THE EFFECT OF SINGING AND VOCAL MUSIC LISTENING ON NEURAL PLASTICITY

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Abstract

Previous studies have shown that vocal music listening supports neural recovery after brain damage, and the ability to sing often remains for patients with aphasia. These findings have raised the need for further investigations on neural activation and post-damage reorganization induced by vocal music. Previous studies on neural correlates of singing have mainly been focusing on professional opera singers and the effects of individuality in music experiences and responses to music on neural activation have been understudied.

The aim of this research is to identify core regions and functions for singing and vocal music processing considering the impact of individual experiences on neural activation. The research focused on singing experience, vocal music exposure in aphasia rehabilitation and individual responses to music. Research method used in this thesis is a mapping review.

Based on the findings in this review the key brain regions for further investigations are insula, and arcuate fasciculus, as they are core areas for both, language processing, and experience-dependent plasticity related to singing. Further investigations on the details of language processing in relation to vocal music could serve to improve the efficiency of neural rehabilitation methods. Neural activation is affected by the familiarity and liking of music, which should also be considered when designing musical interventions. Further investigations based on the results of this research could also add to the lacking knowledge about adult brain plasticity and singing experience, considering the genre-related differences.

Key words: vocal music, singing, neural plasticity, insula, arcuate fasciculus, aphasia

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Tiivistelmä

Aiemmat tutkimukset ovat osoittaneet, että vokaalimusiikin kuuntelu tukee hermoston toipumista aivovaurion jälkeen, ja että kyky laulaa usein säilyy jopa potilailla, joilla on afasia. Nämä löydökset ovat nostaneet esiin tarpeen jatkotutkimuksille liittyen vokaalimusiikin aikaansaamaan neuraaliseen aktivaatioon ja aivovaurion jälkeiseen uudelleenorganisoitumiseen. Aiemmat tutkimukset liittyen laulun neuraalisiin vasteisiin ovat keskittyneet pääasiassa oopperalaulajiin, ja yksilöllisten musiikkikokemusten ja musiikillisten reaktioiden vaikutusta on tutkittu vähemmän.

Tämän tutkimuksen tavoitteena on tunnistaa keskeiset aivoalueet ja toiminnot laulamiselle ja vokaalimusiikin prosessoinnille ottaen huomioon myös yksilöllisten kokemusten vaikutuksen hermoston aktivoitumiseen. Tutkimus keskittyi harjaantuneisuuteen laulamisessa, vokaalimusiikin kuunteluun afasiakuntoutuksessa ja yksilöllisyyteen reaktioissa musiikkiin. Tutkimusmetodi on kartoittava kirjallisuuskatsaus.

Katsauksen löydösten perusteella olennaisimmat aivoalueet jatkotutkimuksien kannalta ovat insula ja arcuate fasciculus, sillä ne liittyvät keskeisinä alueina sekä kielelliseen prosessointiin, että laulukokemuksesta riippuvaiseen plastisiteettiin. Lisätutkimukset laulumusiikkiin liittyvän kielellisen prosessoinnin yksityiskohtien selvittämiseksi voisivat tukea neurologisen kuntoutuksen menetelmien kehittämistä. Hermostolliseen aktivaatioon vaikuttaa musiikin tuttuus ja miellyttävyys, mikä tulisi myös ottaa huomioon suunniteltaessa musiikillisia interventioita. Tämän tutkimuksen tulosten pohjalta ehdotetut jatkotutkimukset voisivat myös lisätä tietoa lauluharjoittelun tuottamasta plastisiteetista aikuisen aivoissa huomioiden eri musiikin lajien ominaispiirteet.

Asiasanat: vokaalimusiikki, laulu, plastisiteetti, insula, arcuate fasciculus, afasia

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1 INTRODUCTION

In this thesis my aim was to study the effects of vocal music and singing on neural plasticity and post-damage reorganization in the brain. Plasticity refers to the neural changes in the brain induced by experiences and changes in the environment. Neural reorganization reflects the brain's adaptation to the deterioration of neurons and neural connections because of brain injury, tumor, or degenerative disease. I've approached the research problem via mapping the brain regions and neural connections related to singing and vocal music listening. The research process continued with a review of studies on vocal music interventions. In this research I've also investigated how the memory function and language processing may impact neural plasticity induced by vocal music exposure, and how individuality in the neural organization and music experiences should be considered when planning vocal music interventions.

Research questions for this thesis were: (1) Which brain areas and functional connections are affected by singing and vocal music listening? (2) What kind of reorganization of the brain structures and functions has been perceived because of song listening or singing interventions? and (3) What kind of limitations and individual factors should be taken into consideration when utilizing and assessing the effects of vocal music or singing in language rehabilitation? The findings on individuality in neural organization and types of damage were reinforced with reviewing studies on the effects of personal music experiences and preferences on neural plasticity.

The research process provided an overview on the current state of research in neuroscience of singing and revealed several gaps in knowledge. Knowledge on the neural activation during singing and vocal music listening is still lacking, and the ongoing development of neuroscientific measurement methods will open new opportunities to approach this topic, proceeding from mapping the regions of interest to studying the connections within and projecting from these responsive areas. This research has shed some light to the needs of further investigation on individual factors related to neural rehabilitation utilizing vocal music, specifically focusing on vocal music listening in aphasia rehabilitation. When it comes to the viewpoint of neural

rehabilitation, this research serves to developing the rehabilitation methods via acknowledging and considering the individuality of a patient as a vocal music listener with personal musical history and preferences.

This research combined knowledge from neural correlates of singing and vocal music listening with findings from neural rehabilitation. Third viewpoint to this topic came from music psychology, as the individual music experiences and responses to vocal music and neural processing of songs were considered as potential factors to affect the outcomes of interventions. By combining findings from recent studies in neuroscience, music psychology and neural rehabilitation, the findings in this research provide tools for development of personalized vocal music interventions in neural rehabilitation settings. Several gaps in knowledge were highlighted in this research, and the Discussion and Conclusions - chapter provides four proposals for future studies to add to the lacking knowledge. The study proposals have been designed to examine the activation of core regions insula and arcuate fasciculus, language processing and the effects of familiarity in vocal music listening and the experience-dependent plasticity related to the regular singing training in adulthood.

2 METHODS

2.1 Aim of the thesis

The aim of this thesis was to find out how singing and vocal music listening affect the neural plasticity. This thesis had a pragmatic approach to the topic, with the improvement of efficiency in music-related neural rehabilitation methods as a goal, along with identification of gaps in knowledge. This was done by finding out how singing and listening to vocal music activates the neural networks in the brain, and how these musical activities can support the neural reorganization and positive plasticity after the brain has been damaged. The findings in this thesis add to the increasing knowledge about the factors affecting the outcomes of vocal music interventions. The findings also clarify the overall potential and challenges of vocal music interventions.

To add some background to the potential of utilization and expected outcomes of singing and vocal music interventions, one of the objectives for this thesis is also to form an overall view on the effects of singing experience and vocal music on the neural plasticity in general. The predictability of efficiency in utilizing vocal music for neural rehabilitation is considered by acknowledging individual features in neural organization and in the type of damage on the brain.

Aiming to add to the existing knowledge on music-related neural rehabilitation, this research moves forward towards personalized vocal music interventions by acknowledging the specific potential of music with lyrics. Considering especially the significance of vocal music in memory processing, and individually shaped musical experiences of the patient, this research considers how and why the effects of singing and vocal music listening should be investigated further. The significance of music preferences is also considered in this thesis, as it may add to the expected outcomes and success of interventions.

Based on the findings in this thesis, interventions can be developed further towards the most effective way of supporting the neural recovery process. In other words, the increased knowledge gained from this research will add to the predictability of success in interventions utilizing vocal music by mapping the individual features and responses of the neurological patients that may affect the outcomes.

2.2 Background and justification of the method

The neural basis of singing is still a challenging and understudied topic. While the existing studies have been able to identify some of the critical structures and connections in the brain, the overall understanding about the neural processing and plasticity related to singing is still lacking, especially considering the different genres of singing and the effects of music taste on neural activity and plasticity induced by singing. The success in therapeutic and rehabilitative use of singing has increased the need for deeper understanding of the recovery process. Combination of the findings about experience-dependent plasticity and findings from rehabilitation studies could form a basis for future research on neural plasticity induced by processing of vocal music.

Previous research on the topic of neural reorganization induced by vocal music listening consists of experimental and qualitative studies in which the number of participants is often relatively small ($N < 100$). Even with well-designed research, this sets a challenge to the reliability and generalizability of the findings. The challenge can be expected to remain in the future, as the new groups of potential participants often appear unexpected after a sudden brain injury, are especially vulnerable, and the individuality in neural organization and responses to the treatment may affect the outcomes of any intervention.

The goal for this thesis was to combine main findings of these studies on this topic to find out if and how they support or contradict with one another, and if they add to the generalizability of the results as such. This thesis also sheds some light on the findings about individual factors that should be considered when utilizing vocal music interventions. The mapping review as a research method served the need to integrate existing knowledge and identify the knowledge gaps.

2.3 Epistemology

This thesis is relying on the post-positivistic view on the nature of knowledge, acknowledging that the objectively measured and described existence of truth is based on imperfect understanding of it (Williamon, Ginsborg, Perkins & Waddell 2021, chpt

1.2.1). The aim of this thesis is pragmatic; to find out how vocal music related rehabilitation methods and interventions could be made more effective, especially for patients with aphasia (PWA). Also based on the pragmatic approach, the hypotheses in this thesis are predictions based on the previous findings, and the support to them has been reported during the research process (Williamon et al. 2021, chpt 1.2.3).

2.4 The research method

The research method used in this thesis was a mapping review. The description of mapping review according to Grant & Booth is to: "map out and categorize existing literature from which to commission further reviews and/or primary research by identifying gaps in research literature" (Grant & Booth, 2009). In this research, this includes gathering the current literature and combining the findings about neural plasticity related to singing and song listening, categorizing them in under subtopics and identifying the needs for further investigations on this topic.

The mapping review was conducted in two parts. The aim of the first part of this review was to form an overall picture on the current state of knowledge and research on the neuroscience and neural rehabilitation related to singing and song listening. The second review was a deepening one, and the focus was turned from neural rehabilitation in general to aphasia rehabilitation, of which there's previous literature available and ongoing research with promising results from brain imaging studies. At this phase the language processing in vocal music became a topic of interest for this thesis also. The reviewed material consisted of qualitative, as well as experimental and quantitative studies, and previous literature reviews. Hypotheses for this thesis were formatted based on the previous knowledge about brain plasticity related to singing and vocal music listening experience, and vocal music utilization in neural rehabilitation.

The papers included in this study were divided into four groups of subtopics: (1) neural activation in singing and vocal music listening, (2) vocal music utilization for neural rehabilitation, (3) language processing in singing and vocal music listening, and (4) emotional and memory processing of vocal music. During the review process the use of vocal music listening in aphasia rehabilitation was chosen for closer investigation. Due to the limited focus of this thesis, the literature focusing on using musical elements instead of whole songs and compositions, such as in melodic intonation therapy (MIT), were mostly excluded from this review.

The mapping review concludes by discussing the main findings in this review. Suggestions are made on how vocal music utilization could be made more effective by combining findings on neural basis of singing and song listening with the potential in neural reorganization, also considering the effect of musical experiences and responses to vocal music. This review also enlightens the current knowledge gaps to be considered in further investigations around this topic.

3 WHICH BRAIN AREAS AND FUNCTIONAL CONNECTIONS ARE AFFECTED BY SINGING EXPERIENCE?

3.1 Hypothesis 1: Singing experience induces structural changes in the brain regions related to voice production

3.1.1 Sensitive period for experience-dependent brain plasticity for singers

When investigating the brain plasticity induced by musical experience, the neural activation and structural changes have often been found to be task-related and instrument-specific. Singing differs from instrument playing as it's a common activity for most people, even without any formal training. Thus, most of laypeople would be expected to have experience-dependent brain plasticity induced by singing, often with relatively accurate pitch.

Janata & Parsons describe singer as a producer and a perceiver, considering that the perceiver may also be producing covertly (Janata & Parsons 2013, 311). This probably is a reliable description for most people and points out the difference between singing and playing an instrument; perception of singing may induce covert singing since it's a familiar activity for most, whereas perceiving someone play violin probably wouldn't induce covert playing unless the person has previous experience in playing the same instrument. Considering the number of laypeople with some experience in singing, the investigation of brain plasticity related to singers calls for participants with significant amount of experience of singing, trained professionals.

From brain plasticity point of view, it's interesting and important to consider that formal training of singers begins significantly later than that of instrumental musicians. Singer training usually doesn't begin earlier than as a teenager or at least after the acute phase of voice mutation. As such, the relationship between the phase of cognitive development and beginning of formal training differs from that of instrumentalists. Kleber et al. have suggested that there may be a sensitive period for the

beginning of formal training of singing, since they found that the structural changes in opera singers´ brains were most significant when they had started formal training not before the age of 14, but as early as possible after that (Kleber, Veit, Moll, Gaser, Birbaumer et al., 2016).

3.1.2 Neural correlates for singing

According to review article by Zarate, the sensory-motor control of singing pitch and can be divided into different subfunctions and responsive brain regions; posterior superior temporal sulcus (pSTS) and intraparietal sulcus (IPS) are related to auditory processing and transformation for motor output, while somato-sensory processing is located to primary somato-sensory area S1 (Zarate, 2013). Zarate also adds that vocal motor preparation and response initiation is located to the dorsal premotor cortex and anterior cingulate cortex. According to Vines et al. the right inferior frontal gyrus (rIFG) is critical in mapping sounds in singing (Vines, Norton & Schlaug, 2011).

TABLE 1: Responsive brain regions in singing

Function	**Responsive brain regions**
Auditory processing and transformation for motor output	posterior superior temporal sulcus (pSTS), intraparietal sulcus
Somato-sensory processing	Primary somato-sensory area (S1)
Vocal motor preparation and response initiation	Dorsal premotor cortex (dPMC), anterior cingulate cortex (ACC)
Mapping sounds in singing	Right inferior frontal gyrus (rIFG)
Production of singing	Right Insula
Auditory-motor integration	Anterior insula
Somato-sensory feedback gating	Anterior insula
Song listening and observation	Right insula
Non-lyrical singing	Right insula
Imagery singing	fronto-parietal region, S1, S2, prefrontal areas, cerebellum
Recall of melody	Right insula
Song recognition facilitation	Left posterior inferior cortex

Functional changes related to singing have been studied when investigating rhythmic brain activity. Gunji et al. compared continuous vocalization to speaking, humming and imagery singing, and found most significant differences in alphaband in right premotor cortex (rPM), bilateral sensory-motor cortex (S1, right secondary sensory-motor cortex (rS2) and bilateral superior parietal cortex (sPC) (Gunji, Ishii, Chau, Kakigi & Pantev, 2007). They also found differences in beta band in PM, S1 and S2 areas, and bilateral superior parietal area, the latest as a common feature with imagery

singing condition. Imagery singing has also been studied with fMRI, having professional (opera) singers as participants, and the activation was perceived on fronto-parietal region, as well as S1 and S2 areas (Kleber, Birbaumer, Veit, Trevorrow & Lotze, 2007). In their case study, Zaytseva et al. also found activation for prefrontal areas and cerebellum in active imagery singing condition. (Zaytseva, Gutyrchik, Bao, Pöppel, Han et al., 2014). (See Table 1)

Experience-dependent plasticity in singing has been studied by Kleber et al. (2016). They used fMRI to study structural changes having opera singers as participants. Increased gray matter volume was found in right ventral primary somatosensory and adjacent rostral supramarginal gyrus, right secondary somatosensory cortex, and primary auditory cortex (Kleber et al., 2016). Halwani et al. studied effects of musical training on arcuate fasciculus (AF) and found that for singers the volume in the left dorsal and ventral branch of AF was higher, but fractional anisotropy value lower for singers than for instrumentalists, and both were higher for singers than for non-musicians (Halwani, Loui, Rüber & Schlaug, 2011). Halwani et al. also suggested that these features on singers are related to sound perception and sound production, as well as to the feedback and feedforward control.

While instrumentalists gain expertise in motor control of limbs used for playing violin or piano, professional singers develop their control of voice and body based on the auditory and somatosensory feedback. In addition to the control of vocal apparatus from neck above, the years of practice include continuous observation and control of core muscle activity, especially in the core-muscles supporting and maintaining ideal state of body for flexible voice production. Singers and singing students also learn by listening, and observing other singers perform. Based on the findings mentioned above, the singing experience induces plasticity changes in auditory and somatosensory cortices, and arcuate fasciculus. Experience-dependent plasticity has also been found in insula area, which will be discussed in the following chapter.

3.1.3 Summary

Singing seems to activate a wide network of brain regions from auditory and somatosensory areas to insula, and white matter tract arcuate fasciculus. Experience-dependent structural changes in insula could be suggested to reflect neural activation related to the different processes in production of singing. Some of the structural changes have related to a sensitive period for the beginning of formal training. This raises questions on how the later onset of training might affect experience-dependent plasticity; the decrease of gray matter and increase of white matter towards adulthood suggests that investigations on the experience-dependent plasticity for adults could be directed towards exploring the white matter connections between regions.

Hypothesis 1 suggests that singing and vocal music listening induces structural changes in the brain regions related to voice production. Indeed, there have been several structural plasticity changes that have been correlated with experience in singing,

and some of the neural correlates have also been related to vocal music listening and imagery singing. Singing experience has been related to the increase of GM volume in right ventral primary somatosensory gyrus, adjacent rostral supramarginal gyrus, right secondary somatosensory cortex, and primary auditory cortex. On the contrary, decrease of gray matter volume in insula has also related to singing experience. Left arcuate fasciculus is also affected by singing experience, and the experience-dependent plasticity has been perceived as higher fractional anisotropy than for non-musicians, and as higher white matter volume in dorsal and ventral branch, than for instrumentalists.

3.2 Hypothesis 2: Insula is a core area for experience-dependent plasticity in professional singers

3.2.1 Insula activation in singing-related functions

Insula area is highly connected including significant efferent connections, and it has been found to show activation for various functions from homeostasis and survival, such as perception of pain, to self-perception and language processing. According to Ardila et al., left insula is notably larger than the right for most humans. They suggest that, from connectivity point of view, insula is the core area for language functions. In their meta-analytic connectivity study Ardila et al. found that insula is participates in e.g., production and understanding of language, repetition, and lexico-semantic associations (Ardila, Bernal & Rosselli, 2014). Moreover, Dionisio et al. found strong connections from the dominant insula to language-motor and association areas (Dionisio, Mayoglou, Cho, Prime, Flanigan et al., 2019). Ardila et al. related the anterior part of the insula to the organization, planning and initiation of language articulation, while posterior part of the insula would be connected to lexical knowledge, word retrieval, language understanding and word discrimination (Ardila et al., 2014).

From singing point of view some of the most interesting processes are the auditory and language functions, especially when lyrics are involved. However, the significance of insula activation in singing may also arise from processes related to interoception and perception of self. Neural activation in insula area has been the related to the production of singing (Jeffries, Fritz & Braun, 2003) (Peretz, Gagnon, Hébert & Macoir, 2004) (Janata & Parsons 2013, 315), auditory-motor integration and somatosensory feedback gating (Zarate, 2013), but also to song listening and observation (Fogassi 2013, 104) (see Table 2). Increased activity in insula during singing has been combined with activation in right anterior superior temporal sulcus (aSTS) (Jeffries et al., 2003) (Peretz et al., 2004).

TABLE 2: Experience-dependent structural plasticity in singers

Region	**Structural change**
Right ventral primary somatosensory gyrus	Increased GM volume
Adjacent rostral supramarginal gyrus (SMG)	Increased GM volume
Right secondary somatosensory cortex (rS2)	Increased GM volume
Primary auditory cortex (A1)	Inreased GM volume
Insula	Decreased GM volume
Left arcuate fasciculus	Higher WM volume in dorsal and ventral branch
Left arcuate fasciculus	Higher fractional anisotropy

3.2.2 Lateralization of insula

Considering the neural processing of speech and song, Janata & Parsons hypothesized that speech production is predominantly lateralized to the left insula, and song production to the right (Janata & Parsons 2013, 315). They also specified that the production of singing is related to the activation of right mid-insula. The lateralization of musical processing to the right was also already found when right temporal lobe resection was found to lead to impaired recall of melody, while left temporal lobe resection resulted in impaired recall of text in spoken and sung form (Samson & Zatorre, 1991, in Janata & Parsons 2013, 321).

According to the CCEP-study by Dionisio et al., both insulas have connections to primary auditory cortex, and strong connection to secondary auditory cortex. They also found that the connection to Heschl's gyrus is weak, which may suggest that insula plays a role in the integration of auditory information. Language seems to be lateralized to the left insula, at least for patients whose language processing is dominantly lateralized to the left. There are strong connections from the dominant insula to language-motor and association areas, and the non-dominant insula also projects to the contralateral language areas. Language lateralization can also be seen in right insula activation for non-lyrical singing. This supports the hypothesis of Janata & Parsons about song production lateralization to the right (Janata & Parsons 2013, 315). Dionisio et al. also suggest that the left insula may enhance the activation of right insula in non-lyrical singing, or that there may even be suppression of left insula when there are no lyrics. (Dionisio et al., 2019)

To provide some support to the significance of insula area for singers, Janata & Parsons already suggested that the experience in linguistics or music may affect the lateralization of speech and song production in insula (Janata & Parsons 2013, 315). The experience-induced plasticity changes in insula have indeed been related to professional singers by Wang et al., who found that decreased gray matter volume in insula correlated with efficiency in sensory-motor control for vocal production (Wang, Wei, Chen, Jones, Gong et al., 2019). Wang et al. also suggested that the insula area might be independent from auditory areas since the professional singers are not easily distracted by manipulated auditory feedback.

Insula and its independence from auditory areas has been evaluated by disturbing auditory feedback with noise. This was done in the study by Kleber et al., who found increased right anterior insula activation for trained singers, but not for untrained singers, in a noise-masked singing task (Kleber, Friberg, Zeitouni & Zatorre, 2017). Based on these findings it seems that insula plays a role in professional singer's inner control of voice when auditory feedback is faulty or lacking. Ardila et al. related the anterior part of the insula to the organization, planning and initiation of language articulation, while posterior part of the insula would be connected to lexical knowledge, word retrieval, language understanding and word discrimination (Ardila et al., 2014).

3.2.3 Summary

The gaps of knowledge about the role of insula in singing seems to be in the connectivity of insula for experienced singers. The need for research methods using non-invasive research methods designed for the challenging anatomy and location of insula is obvious. In the studies chosen for this review, the control of voice has been in the center of investigation, but in case of especially classical and opera singing, it should also be considered that professional singers process lyrics in several different languages regularly in combination with melody and thus gain specific experience in pronunciation and prosody throughout their training and career. This might suggest some plasticity changes for professional singers in processing and learning of languages, which have not yet been investigated, for instance; if and how the insula dominance and lateralization of language processing are affected by singing training, and if the connectivity of insula is affected by singing experience and the bilaterality of singing vs. speech.

The increase of knowledge about the language processing and brain plasticity in singing could provide deeper understanding about the timing and duration of plasticity changes, and the related cognitive enhancements. This could improve efficiency of singing related rehabilitation methods, but also add to the development of formal training for singers. Experimental studies relating to the connections expanding from insula, and to the arcuate fasciculus could provide some cues on how to use vocal training for neural activation also in rehabilitation settings.

Hypothesis 2 suggests that insula is a core area for experience-dependent plasticity in professional singers. This is supported by the findings showing specific structural changes in insula area for professional singers, and insula activation during the production of singing. The activation of right insula has also been related to singing professionals not being distracted in a noise-masked singing task. However, insula is also a core area for language processes, and further investigations should be conducted to find out if insula activation during singing relates to lingual expertise gained in voice training.

3.3 Hypothesis 3: Singing and listening to vocal music with lyrics improves cognitive repair and neural reorganization in language areas after a sudden brain damage

3.3.1 Aphasia – bilaterality of vocal music processing as a tool for neural rehabilitation

Music therapy, singing and vocal music listening have been used for rehabilitation purposes for patients with aphasia (PWA). The most common cause for aphasia is cerebrovascular accident resulting in damage or dysfunction of language-cognitive network, but aphasia may also be caused by traumatic brain injury (TBI), memory illness, neurological disorder, or brain tumor (Klippi, Korpijaakko-Huuhka, Lehtihalmes, Rautakoski, Ahlholm et al., 2017, p. 26-28). Language rehabilitation may induce positive and negative types of plasticity. Positive plasticity refers to neural reorganization and reconnections leading to the recovery of cognitive processes, while negative plasticity refers to faulty connections resulting in unwanted actions and learning, potentially even leading to a state where the patient in rehabilitation doesn't want to try completing any tasks that are demanding. (Klippi et al. 2017, p. 149).

Music listening has been found to support cognitive recovery and mood after middle-cerebral stroke (Särkämö, Tervaniemi, Laitinen, Forsblom, Soinila et al., 2008). The use of vocal music instead of instrumental for language rehabilitation can be justified based on the neural activation of language areas induced by processing music with lyrics. The main areas of language processing, Broca (anatomically left inferior frontal gyrus, IFG) and Wernicke have been located to the left temporal lobe. However, the neural network of language processing depends on the context, and happens in interaction with other functions, such as memory and executive processing (Hultén 2017, p. 16). According to Klippi et al., the neural network related to language processing consists of at least two dorsal and two ventral white matter tracts that connect cortical areas to one another (Klippi, et al. 2017, p. 145).

According to the review by Liu et al. music therapy improves functional communication, repetition, and naming, but doesn't improve comprehension of speech in post-stroke aphasia (Liu, Li, Yin, Zhao, Yang et al., 2022). However, processing of music with lyrics could include associative verbal processing, and the bilaterality of singing has been suggested to be the key to recruiting compensatory language areas in the right hemisphere (Gunji et al., 2007). Right hemisphere activation might also be related to emotional cues provided by songs, and repetition and learning of melody might enhance the mnemonic effect of songs (Leo, Sihvonen, Linnavalli, Tervaniemi, Laine et al., 2019). Leo et al. also suggested that sung melody enables chunking, which makes it easier to combine words, and therefore adds to the fluency of speech.

The efficiency of vocal, instead of instrumental, music listening as a rehabilitation method was already noted by Särkämö et al. when investigating patients with middle-cerebral artery strokes and finding that listening to music enhanced the patients´ recovery of verbal memory, in comparison to patients listening to audio books and the control group which wasn't assigned with any listening material (Särkämö et al., 2008). These improvements were later connected with an increase in gray matter volume (GMV) in frontolimbic areas for the patients that had been listening to music (Särkämö, Ripollés, Vepsäläinen, Autti, Silvennoinen, et al., 2014).

In a more recent study, Sihvonen et al. investigated the effects of vocal music listening on the recovery of poststroke patients, and found that cognitive rehabilitation was more efficient for, especially aphasic, patients who listened to vocal music regularly, compared with patients who listened to instrumental music or audiobooks (Sihvonen, Leo, Ripollés, Lehtovaara, Ylönen et al., 2020). They also found that the effect of daily music listening in poststroke condition was seen as an increase in gray matter volume in left temporal areas, and as an increased functional connectivity in default mode network. Based on these findings they suggested that vocal music listening may prevent atrophy in poststroke condition (Sihvonen et al., 2020).

Melodic intonation therapy (MIT), in which intervals are used for enhancing speech recovery, also aims at recruiting right hemisphere areas to aid in language processing, although it's been considered more useful for apraxia of speech than aphasia (Zumbansen et al., 2014). In the study by Vines et al. (2011) they combined MIT and anodal tDCS to the right inferior frontal gyrus which led to significant improvements in fluency of speech for patients with moderate to severe aphasia (Vines, Norton & Schlaug, 2011). The longevity of the results in this study wasn't monitored, and whether this non-invasive brain stimulation would strengthen the effects of singing or vocal music listening also calls for further investigation.

3.3.2 Damage to the shared networks of language and music impairs processing of both

When utilizing songs for brain damage rehabilitation it's also worth considering that the damaged brain regions may include areas crucial not only for language functions, but for music processing also. According to Vines et al., the right inferior frontal gyrus, activated in sound mapping in singing, has been found to be critical in recovery of aphasia especially when there are large lesions in the left hemisphere (Vines et al., 2011). Sihvonen et al. found that the damage and disconnection in right ventral stream seems to be an underlying factor in both, amusia and aprosodia (Sihvonen, Sammler, Ripollés, Leo, Rodríguez-Fornells et al., 2022). When it comes to vocal music, some areas or connections in the left hemisphere may also be crucial for integration of lyrics and melody since left temporal lobe resection has been found to impair recall of text, whether it's spoken or sung (Janata & Parsons 2013, 321).

Overlapping of neural networks related to language and music has been noted in several studies, including Callan et al. and Moreno (Callan, Tsytsarev, Hanakawa, Callan,

Katsuhara et al., 2006; Moreno, 2009). The common regions for speech and singing include the left planum temporale and the superior temporal parietal region, left and right premotor cortex, lateral aspect of the VI lobule of posterior cerebellum and anterior superior temporal gyrus (Callan et al., 2006). The activation of Broca and Wernicke language processing areas, anatomically referred as left inferior frontal gyrus (lIFG) and posterior superior temporal gyrus (pSTG) (Hultén 2017, p. 15). have also been related to singing (Gunji et al., 2007).

Damage and disfunction to the right ventral stream with lesions in right fronto-insular and striatal areas seem to be fatal for both, music and language processing, since they are common factors underlying amusia and aprosodia (Sihvonen et al., 2022). Sihvonen et al. also found lower tract volume and reduced fractional anisotropy in right inferior fronto-occipital fasciculus (rIFOF) related to condition with amusia and aprosodia. This white matter tract has been previously related to bilateral processing of non-verbal semantics (Herbet, Moritz-Gasser & Duffau, 2017).

Some of the lesion-studies have also shown that amusia and aphasia do not always occur simultaneously. Peretz et al. found that damage to bilateral auditory and right frontal areas correlated with amusia without aphasia (Peretz & al., 2004), which would suggest that these areas are crucial for music processing, but not for language functions. Effects on singing, but not speaking for professional singers have been related to the infarction in right superior temporal gyrus (STG) (Terao, Mizuno, Shindoh, Sakurai, Ugawa et al., 2006) and to the electrical stimulation of right STG (Katlowitz, Oya, Howard, Greenlee & Long, 2017). Terao et al. suggested that the right superior temporal cortex participates in the fine tuning of vocal production, because the acquired impairments seemed to be related to overshooting of high and low notes when attempting to sing large, familiar intervals (Terao et al., 2006).

The advantage of these case studies by Terao et al. (2006) and Katlowitz et al. (2017) has been the ability to evaluate singing capability also before the alterations in neural activity caused by stimulation or infarction. The limitation to both is that the participants were professional singers trying to sing familiar melodies. The processing of long known and novel songs may differ from one another, as will be discussed further in the chapter about the superior memory processing of vocal music.

3.3.3 Vocal music is more than a combination of language and music

Considering the shared networks between language and music it's important to also be able to separate these processes from one another. Some illumination to the differences of verbal and melodic processing and support to the lateralization were provided by Saito et al., suggesting that verbal lexical processing recruits left fusiform gyrus and left inferior occipital gyrus, while melodic lexical processing recruits left fusiform gyrus with bilateral temporo-occipital and temporo-parietal cortex (Saito, Ishii, Sakuma, Kawasaki, Oda et al., 2012).

It would be tempting to suggest that the neural activation process in perception of songs could simply be considered a combination of speech and instrumental music. However, based on findings in a recent study by Norman-Haignere et al., it seems that this may not be the case. For better spatial resolution than superficial EEG, Norman-Haignere et al. used intracranial ECoG to study neuronal responses to different auditory stimuli, including vocal music. They found a specific population of neurons responding only to songs, and not to instrumental music or other sounds, and the sum of component activation was significantly higher than the component sum of neurons responding to instrumental music and speech (Norman-Haignere, Feather, Boebinger, Brunner, Ritaccio et al., 2022). This finding supports the theory about the dual coding of vocal music, including coding of lyrics and coding of lyrics with melody (Peretz et al., 2004). However, the semantic aspects of lyrics may not be coded automatically, as will be discussed later in this thesis, along with the hypothesis about the superior memory for vocal music.

3.3.4 Summary

The advantage of vocal music interventions in language rehabilitation has been related to the activation of compensatory areas in the right hemisphere. Songs provide continuous vocal production supported by the melodic changes and the rhythm of music. Chunking of words in sung melody may add to the fluency of speech. Right hemisphere activation has also been related to emotional processing. The significance of right hemisphere activation for speech improvements has also been found when supporting MIT with excitatory stimulation of rIFG.

When it comes to neural plasticity, listening to music has been found to enhance patients' recovery of verbal memory in case of recovering from middle-cerebral artery strokes. This improvement was related to increased GM volume in frontolimbic areas. When comparing regular listening of vocal music or instrumental music, it was found that the cognitive rehabilitation of post-stroke patients was more efficient for patients with aphasia who listened to vocal music. This was related to an increase in GM volume in left temporal areas and increased functional connectivity in default mode network. Aphasia is most often related with damage to the left temporal areas, and vocal music listening has been suggested to potentially prevent atrophy in this area in post-stroke condition.

The shared network of language and music promotes, but also challenges expectations of success when utilizing musical interventions for language impairments. Symptoms of amusia and lesions in the areas related to music processing may underlie the unsuccessful interventions and rehabilitation methods. Aprosodia could be the result of the damage to the right ventral stream and frontoinsular and striatal areas, which are also related to amusia. Lower tract volume and reduced fractional anisotropy in right IFOF have also been related to both of those conditions. Infarction in

rSTG has been related to impairments in singing for professional singers, which suggests that it may also alter the outcomes of singing interventions.

Singing and listening to vocal music seem to be promising ways of supporting neural recovery in the language areas, especially by activating the compensatory language areas in the right hemisphere. Cognitive improvements and positive plasticity can be expected to emerge already after regular vocal music listening for poststroke patients. Amusia and lesions in the related brain regions may set limits to the success in utilizing musical interventions, if the functional connections and areas needed to process the music are impaired. The positive outcomes of vocal music listening and singing interventions may also be affected by emotional and motivational factors related to self-selection and responses to music, as well as to the musical experiences and semantic processing of lyrics, which will be discussed in the following chapter.

Hypothesis 3 suggests that singing and listening to music with lyrics improves cognitive repair and neural reorganization in language areas after a sudden brain damage. This has been supported by the findings showing that listening to vocal music enhanced cognitive repair for PWA more than listening to instrumental music or audiobooks. The details of this supportive process remain unclear, as the patients listened to self-selected music which may also be motivational and provide emotional support. However, the improvements were correlated with an increase of GM volume in left temporal areas and increase of functional connectivity in DMN. The specific effect of vocal music listening may also be based on the activation of specific population of neurons responding to vocal music, but it calls for further investigation whether the activation of this population is playing a significant role in the process of neural recovery.

4 WHAT KIND OF LIMITATIONS AND INDIVIDUAL FACTORS SHOULD BE TAKEN INTO CONSIDERATION WHEN UTILIZING AND ASSESSING THE EFFECTS OF VOCAL MUSIC OR SINGING IN LANGUAGE REHABILITATION?

4.1 Hypothesis 4: Individual differences in the type of lesion and neural organization of the brain may affect the outcomes of vocal music interventions for patients with aphasia

4.1.1 Individual experiences affect plasticity

While there have been several promising findings about cognitive, social and language improvements induced by vocal music listening and singing (Särkämö et al., 2014; Mansens, Deeg & Comijs, 2018; Sihvonen et al., 2020; Fischer, Churchill, Leggieri, Vuong, Tau et al., 2021; Dassa & Amir, 2021), some individual features of the participants should be considered before generalizing vocal music interventions as efficient for all people with similar diagnoses. The effects of new experiences on the brain plasticity may also vary according to brain structures and functions that have been shaped by development and individual life experiences.

Even though damage to some specific brain regions have been related to certain types of symptoms and impairments, such as left temporal lobe damage is often the underlying cause of aphasia, the type and extent of damage may vary individually. Lesions in same areas may also cause different symptoms for different people, and the same symptoms can be results of lesions in different areas for different people (Klippi et al. 2017, p. 41).

4.1.2 Neural reorganization in aphasia

The effect of vocal music interventions on language impairments has been assumed to be based on bilateral processing and right hemisphere activation compared to dominantly left lateralized verbal processing without music (Peretz et al., 2004; Vines et al., 2011; Saito et al., 2012). In case of aphasia, the damage to the left hemisphere results in the right hemisphere activation, returning to left hemisphere if rehabilitation is successful and language network is normalized (Klippi et al. 2017, p. 150).

Klippi et al. suggest that the rehabilitation methods in the acute phase of aphasia should concentrate on the language, considering the significance of spontaneous recovery that is strongest during the first 30 days (Klippi et al. 2017, p. 147-152). In a music therapy review by Liu et al. it was noted that more improvements induced by music therapy were seen in a subacute phase of poststroke aphasia, than in the chronic phase, which suggests that the timing of intervention may play a significant role in the recovery process (Liu et al., 2022). Sihvonen et al. also found promising effects of music listening for patients in a subacute phase of aphasia (Sihvonen et al., 2020).

4.1.3 Type of damage affects the lateralization of compensatory language areas

Singing and song listening has been thought to support the activation of compensatory language areas in right hemisphere. However, lesion in the left temporal lobe doesn't automatically result in language lateralization to the right. Lateralization of language areas to the right is most likely in sudden brain damage, such as strokes, but in case of slowly growing tumors the nearby ipsilateral areas may act as compensatory areas if they are intact, and only the white matter tract arcuate fasciculus may be lateralized to the right (Pasquini, Di Napoli, Rossi-Espagnet, Visconti, Napolitano et al., 2022). Based on this it could be assumed that musical interventions could be most efficiently utilized for patients suffering from sudden brain damage to the left hemisphere language areas, since the recovery process includes activation of compensatory language areas in right hemisphere, and the bilateral activation could be supported with musical stimuli.

Connectivity of white matter tracts has been highlighted in recent years (Klippi et al. 2017, p. 41) and the thickness of the right lateralized long segment of arcuate fasciculus (AF) has been related to successful recovery of aphasia (Klippi et al. 2017, p. 151). Thinness of the arcuate fasciculus section terminating in superior temporal gyrus (STG) in the right hemisphere has been related to amusia (Janata & Parsons 2013, p. 320). Based on these findings, monitoring the thickness of essential sections of arcuate fasciculus could add to the expectations on success of musical interventions.

Activities that strengthen this white matter tract AF connecting language areas Wernicke and Broca, could serve the recovery process especially when language functions are impaired. Music may be such an activity, since musicians have been found to have larger volume and fractional anisotropy in arcuate fasciculus, than non-musicians. Halwani et al. also found that singers have larger tract volume on the left arcuate

fasciculus terminating in STG, than non-musicians, but for instrumentalists the fractional anisotropy value was larger in this area. This trend was also found to exist in the left ventral part of arcuate fasciculus, expanding from middle temporal gyrus (MTG) to inferior frontal gyrus (IFG). (Halwani et al., 2011)

4.1.4 Effects of handedness, native language, and environment

Based on these findings, the timing and type of lesion and intervention, but also the symptoms of amusia should be considered before applying musical interventions. The starting point in neural organization before the brain damage may also affect the outcome of rehabilitation, but in case of sudden brain incidents only the state after the damage is monitored and the individuality in neural organization can only be assessed based on the personal experiences and interests, such as musical background. However, at the early stage of degenerative disease or a growing tumor, the potential to monitor the progress of damage, and the effects of rehabilitation may provide a tool for assessing the potential support of different rehabilitation methods to neural reorganization.

Individual differences in functional and structural lateralization may also affect the successfulness in applying different rehabilitation methods. When considering the lateralization of language, for 25-30% of (mostly left-handed) people the functions are bilateral or lateralized to the right to begin with (Klippi et al. 2017, p. 27), and the effects of vocal music stimulation could differ from those with left lateralized language functions.

There may also be some differences on the neural organization depending on the native language of the person. Fan et al. found that for Chinese people the lesion distribution related to poststroke aphasia and speech comprehension deficits is significantly different from English speaking ones, often correlated with lesions in sensorimotor areas (Fan, Gao, Zhang, Xin, Sang et al., 2021). These regions have also been found to activate in singing (S1) and imagery singing (S1, S2) conditions (see table 1). There may also be some specific challenges in rehabilitation if the patient is bilingual, even though there may also be transfer effects from one language to another in lingual rehabilitation (Klippi et al. 2017, p. 61).

The use of vocal music in general is also related to the culture, which leaves an open question about cultural factors and their effect on vocal music interventions. The success of rehabilitation also depends on the patient´s social environment and individual ways of responding (Klippi et al. 2017, p. 358), and on the accessibility to rehabilitation in general, which may also vary depending on the department of care (Klippi et al. 2017, p. 345).

4.1.5 Summary

Individuality in neural organization and accessibility of rehabilitation sets a challenge to successful aphasia rehabilitation. When it comes to language impairments, the native language may result in differences in neural organization. Even though the language is dominantly processed in the left temporal lobe by most people, for a significant minority of people this is not the case, and language processing is highly bilateral or even dominantly lateralized to the right.

Connections between language impairments and types of brain damage are ambiguous, as the type of damage varies individually, and the critical disfunction may also be related to the crucial regions, but also to the crucial connections between regions. According to the papers reviewed in the following chapter, bilaterally activating vocal music interventions are assumed to recruit compensatory language regions from the right hemisphere, and thus they can be expected to support recovery process that includes this kind of compensatory activation, such as sudden brain damage. Timing of the intervention seems to make a difference, as most improvements have been perceived in the subacute phase of recovery, after the spontaneous recovery during the first 30 days after the injury.

The state of white matter tract AF connecting Broca and Wernicke seems to predict aphasia recovery. This tract may also affect the outcomes of musical interventions, as it also seems to be affected by musical training and experience in singing on healthy people, and some structural features have also been related to amusia. Whether vocal music interventions would serve to strengthen and this tract, calls for further investigation.

The hypothesis 4 suggested that individual features in the type of lesion and neural organization of the brain may affect the outcomes of vocal music for patients with aphasia. This was supported by the findings that damage to crucial structures and connections to both, music, and speech, can also override the supportive effect of vocal music on neural recovery. Neural organization is also individually formed to begin with, and the neural correlates, as well as the crucial structures may differ depending on the native language.

The potential for utilizing music to support neural rehabilitation may also be affected by the timing, type, and progress of the damage. The support of music listening for neural recovery of PWA has been assumed to be based on the activation of compensatory areas in the contralateral side of the brain, and this type of activation has been related to sudden brain damage. In case of slow progressing tumor, the recovery of critical functions may not include activation on the contralateral, but on the ipsilateral side of the brain. It calls for further investigations whether vocal music listening would still support the neural reorganization if activation of right hemisphere compensatory areas isn't an essential phase of the recovery process.

4.2 Hypothesis 5: The memory traces formed by vocal melodies are stronger than those of instrumental melodies

4.2.1 Significance of vocal vs. instrumental music in memory

Probably the most obvious difference between listening to instrumental music and songs with lyrics is the presence of human voice and language. The connection between songwriter or performer and the listener could be strengthened via congruent lyrics. The specific significance of vocal vs. instrumental music has also been found in cognitive rehabilitation studies using self-selected music. In the music listening for rehabilitation study by Fischer et al., the participants with mild cognitive impairments were asked to self-select long-known music that was significant to them, and most of the music chosen was vocal (Fischer et al., 2021).

Retrieval of familiar songs and artists is a quick process; according to Janata & Parsons it only takes about 300-400ms (Janata & Parsons 2013, p. 324). Superior memory for vocal vs. instrumental music is already well-known, but the basis of this phenomenon calls for further investigation. The following findings show how the memory for vocal melodies is superior to the instrumental ones even when memory process could be affected by musical experience or motor distraction, but also how a violation to expectation can be detected already when changing the melody for a single word. These findings provide some support to the hypothesis about the superiority in memory for vocal music being based on the melody, or combination of melody and voice, rather than on the semantic content of lyrics.

4.2.2 Subvocal training might underlie the superior memory for vocal music

Superior memory for vocal music seems not to be affected by musical experience, even though musicians have often had significant exposure to timbres of other instruments as well. Weiss et al. aimed to study if the superior melody for vocal music was based on more significant exposure to singing voice over other timbres, and if having absolute pitch might affect the memory. They found out that having absolute pitch didn't affect the superiority of memory for vocal melodies, and the memory of the participants was better for vocal compared with piano melodies even when the participants were professional pianists and had been extensively exposed to piano melodies as such (Weiss, Vanzella, Schellenberg & Trehub, 2015).

Some support to the unique memory processing of songs also comes from an earlier case study with Peretz et al., in which a patient with symptoms of amusia and progressing dementia was able to recognize familiar songs even when they were presented without lyrics, but unable to recognize familiar instrumental music (Peretz et al., 2004). In this case the patient was also able to sing, which might suggest that the memory of vocal melodies could be supported by inner singing. This was also

suggested by Janata & Parsons, who found that familiar songs activate an extensive network, which might be partially due to covert singing (Janata & Parsons, 2013, 323). Sihvonen et al. also suggested that subvocal training might underlie the enhanced cognitive recovery after song listening in poststroke condition compared with listening to audiobooks or instrumental music (Sihvonen et al., 2020). They also suggested that vocal music listening might recruit frontotemporal network more effectively.

Weiss et al. tried to investigate whether the memory processing of vocal melodies could be disturbed by simultaneous motor distractions, but found out that the chosen distractions, such as tapping or humming while listening, didn't affect the superiority of memory for vocal melodies (Weiss, Bissonnette & Peretz, 2021). Discussion in this study suggest that either the memory for vocal melody isn't based on inner singing, or the distractions used in this study might not have been drastic enough to disturb it.

4.2.3 Memory processing for lyrics and melody

Superior memory for vocal melodies could be explained by dual coding of (1) lyrics and (2) lyrics integrated with melody (Peretz et al., 2004). This theory also suggests why motor distractions applied in the study by Weiss et al. (2021) weren't enough to disturb encoding of vocal melodies; the motor distraction should also involve verbal processing to recruit the same network as in the memory task. Singing experience might also add to the recall of vocal melodies, especially if the underlying explanation is inner singing. In the study by Wang et al. they found that the pitch production of professional singers isn't disturbed by external auditory stimuli in an overt singing task (Wang et al., 2019). It calls for further investigation whether the memory processing of vocal melodies is also affected by the singing experience, especially if the inner control in pitch production applies to covert singing also.

Based on their EEG study using single words with sung melodies, Gordon et al. suggest that lyrics are coded automatically, since the ERP response to the word didn't change when participants were asked to pay attention to melody. They also noticed that changing the melody for the sung word elicited stronger N400 response, as a sign of violation to expectation, which provides some support to the instant integration of lyrics and melody in memory processing. Gordon et al. also suggested that the late positive responses may reflect emotional processing. In this study they didn't measure ERPs in "sung melody with no word" – condition, which makes it call for further investigation to conclude whether the late positives could be induced by the sung word, the integration of melody and word, or by the melody sung with human voice, potentially unaffected by verbal or semantic processing. (Gordon, Schön, Magne, Astésano & Besson, 2010)

Familiarity may also affect neural responses in song listening; conflicting with the idea about the dual coding of songs, according to Saito et al. verbal and melodic processing is separate for familiar songs. (Saito, 2012) Saito also suggests, that the left

posterior inferior cortex may facilitate song recognition. Whether and how neural responses could be affected by the familiarity of the performer, recording, or listening circumstances could be investigated in further studies.

The recognition of familiar songs and singing along to them doesn't yet provide information about the processing of the semantics in the lyrics and associations related to them. Janata & Parsons suggested that the semantic processing of lyrics might be separated from musical presentation, since the recognition of words for congruent melody is fast but the semantic content of the lyrics in association with the melody takes time to strengthen (Janata & Parsons 2013, p. 321-323).

4.2.4 Music is prioritized over semantic content of lyrics in memory processing

Based on these findings, the recognition and recall of familiar songs is superior to instrumental music, and not affected by exposure to other timbres induced by musical training. The integration of lyrics and melody seems to be instant and automatic, but independent from semantic processing of language. This suggests that memory processing prioritizes sung phonemes, syllables, or words, but no meaning. This could be related to covert singing and premotor processes in vocal production, but the findings in the studies previously reviewed don't yet fully support this theory, and thus it should be investigated further.

It also calls for further investigation whether, how and in what stage of listening or singing the semantic content of lyrics is stored and how it is recalled, if at all. Enhanced recall of vocal music vs. instrumental seems to be based on the sung melody, but the role of the semantic content in lyrics in the process remains unclear. The irrelevance of semantical congruence of lyrics may also be perceived when considering misheard lyrics; the recalled lyrics may not be semantically congruent, but they are suitable for the melody and listeners may rely on them even they don't make any sense. The physical and emotional aspects of singing should also be investigated further; the superior memory of vocal music might also be based on, for instance, changes in breathing or heart rate while singing or listening to singing.

For therapeutic, teaching or rehabilitation purposes, it would be useful to increase understanding about when and how and if the semantic aspects of lyrics could or should be considered during the training or intervention utilizing songs with lyrics. Emotional content of songs, individual music experiences, and musical autobiography may also affect the processing and recall of semantic content, as will be discussed in another chapter of this thesis. It might also be worthwhile to investigate how significant singing experience of different music genres could affect memory processing of semantic content in lyrics.

4.2.5 Summary

Based on the previous findings, when people are asked to choose significant music to listen to, it's mostly vocal. The recall of vocal melodies is also better than that of instrumental melodies, unaffected by absolute pitch or significant exposure to other musical timbres. Familiar vocal melodies may also be recalled even when the instrumental ones aren't.

The factors that underlie superior memory for vocal music remain somewhat unclear, but subvocal training has often been suggested to be related to the phenomenon, also when vocal music listening has been utilized successfully to induce cognitive improvements in poststroke rehabilitation. It was suggested that vocal music listening might recruit frontotemporal network more effectively, than listening to audiobooks or instrumental music.

The theory about dual coding of (1) lyrics and (2) lyrics integrated with melody is getting some support from the studies aiming to enlighten the memory processing of vocal melodies, but so far, they seem to raise more questions than answers. Motor disturbances, even the musical ones, didn't seem to affect the enhanced recall of vocal melodies over instrumental ones, and the topic of lyrics processing in vocal production and memory processing remains understudied.

The specificity in the recall of songs also arises from the well-known findings and perceptions about elderly people with memory illnesses being still able to recall and sing along to familiar songs. Moreover, same applies to the findings about patients with aphasia unable to speak, but capable of singing and even learning new songs. When it comes to the neural basis of vocal music and singing, they seem to be easy to access, but difficult to remove from the brain. This could be based on the extensive and associative network activated by songs, but the details and the potential of plasticity in this system this still call for further investigation. For rehabilitation purposes, the effects of personal experiences on musical interventions should also be considered, as will be discussed in the following chapter of this thesis.

The hypothesis 5 about the stronger memory traces for vocal vs. instrumental melodies is supported by the findings showing how the enhanced recall of vocal melodies is unaffected by musical experience, and how the familiar melody without lyrics is enough to serve as a priming cue for the recall of a familiar song. The unsuccessful efforts to disturb the memory processing with various distractions raise an assumption about an automatic and associative storing process and it may be even more efficient for professional musicians. Findings reviewed here have also shown how vocal melodies may be recalled even when the instrumental ones are not recognized at all. On some occasions the recall for vocal melodies seems to even override language and memory impairments, as an aphasic incapable of speaking may be able to sing, and a patient with dementia may still be able to sing familiar songs.

4.3 Hypothesis 6: Musical autobiography, musical preferences and aims of music listening affect the reactions to vocal music in neurological rehabilitation

4.3.1 Responses to music are shaped by personal experiences

Taste in music and reactions to music may vary a lot from incapability to enjoy music at all to preferring specific genres, artists, and pieces above all others. According to following findings, our brain responds differently to familiar or unfamiliar music. We might also have strong emotional and physical reactions to music we don't like. When considering vocal music, the contents of the lyrics or the message in the chorus may also affect how well we engage with music or even dance or sing along to it. Music may be used for escapism, it may be sad and comforting at the same time, or it may offer an opportunity to express emotions.

Music may also evoke negative or even traumatic memories that one doesn't want to process at the time, or one may need help in dealing with them. These individual experiences and differences should be considered especially if we utilize music in circumstances where everyone exposed to it aren´t able to express what they want to sing or listen to if anything at all. In the following chapters of this thesis the effects of musical preferences, aversive music, and musical memories on the outcomes of musical interventions in neurological rehabilitation are being evaluated.

4.3.2 Neural correlates for familiarity in music

Listening to self-selected music induces emotions, evokes memories, and gives us pleasure. Music-induced pleasure is a combination of predictability and surprise (Ara & Marco-Pallares, 2021). These predictions and responses to music have been related to the activation on the responding brain regions. According to Rauscheker, anticipation of familiar music activates inferior frontal cortex (IFC), and anticipatory imagery of familiar music also activates cerebellum and anterior cingulate cortex (ACC) (Rauscheker 2003, p. 360). Rauscheker also suggests, that anterior superior temporal gyrus (aSTG) and orbitofrontal cortex (OFC), that process complex auditory patterns, are related to musical memories.

Activation of brain areas may also vary according to the liking of music; highly pleasing, self-selected music activates anticipatory and reward systems dorsal and ventral striatum, and basal ganglia (Salimpoor et al., 2011, in Janata & Parsons 2013, p. 316). Ara & Marco-Pallarés found that pleasure induced by liked familiar songs is significantly higher, than the pleasure induced by liked novel songs (Ara & Marco-Pallarés, 2021). This finding highlights the impact of personal music experiences on the outcomes of music listening. The specific impact of familiarity on neural activation is supported by Janata & Parsons, suggesting that activation spreads into even further areas for memory evoking songs, such as dorsal medial prefrontal cortex (dmPFC),

which has also been related to autobiographical memory and self-representation (Janata & Parsons, 2013). (See Table 3)

TABLE 3: Responsive brain regions for familiarity and liking of music.

Process	**Responsive region**
Anticipation of familiar music	iFC
Anticipatory imagery of familiar music	cerebellum, ACC
Memory evoking songs	dmPFC
Musical memories	aSTG, OFC
Highly pleasing, self-selected music	dorsal and ventral striatum, basal ganglia

The different responses between liked familiar and liked unfamiliar music can also be seen in the oscillatory activity (see Table 4). Ara & Marco-Pallares found that the combination of the familiar of songs and induced pleasure was related to inter-hemispheric temporo-parietal theta synchronization, while unfamiliar music and pleasure was related to right fronto-temporal theta synchronization (Ara & Marco-Pallarés, 2021). Based on these findings, both, liked familiar and liked unfamiliar music could be utilized to purposely support neural activation in an extent network between different brain regions. The repetitive use of novel songs would also turn the novel song into familiar, and the neural activation could be expected to change accordingly, if the responding regions for music processing are intact.

TABLE 4: Oscillatory activation differences in listening to liked familiar vs. liked novel songs.

Stimuli	**Emotional response**	**Oscillatory activation**
Familiar songs	Pleasure	inter-hemispheric temporo-parietal theta synchronization
Novel songs	Pleasure	right fronto-temporal theta synchronization

4.3.3 Emotional consequences of brain injury

The potential of utilizing vocal music interventions for neural rehabilitation is affected by the type and location of the neural damage, but also by the psychological consequences of the injury. Brain injury has often several effects on patient´s emotion experience and expression. According to Powell, after a severe brain injury the patient may seem self-centered like a 3–4-year-old child. Patient may also be impulsive, uninhibited, irritable, and the emotional control may be weak. These symptoms are often

related with damage in the orbitofrontal area. On the contrary, the damage to the dorsolateral areas may result in apathy, abstinence, and emotional flatness. These symptoms affect not only the patient, but also the family members and other close ones. (Powell 2005, p. 107-143).

Depending on the type and size of lesion, the damage to the orbitofrontal area could also damage the processing of musical memories, which was located partially to this area by Rauscheker (2003, p. 360). This might suggest that the personal music experiences might not be successful tools for rehabilitation, especially if the patient shows symptoms of amusia. However, the musical memories could also activate the intact regions in the damaged area, and thus serve to support the neural recovery and reorganization.

The motivation of the patient and the emotional factors are crucial for successful rehabilitation (Klippi et al. 2017, p. 149-156). Klippi et al. also mention that for chronically aphasic patients the lingual impairments may result in reduction of social contacts and isolation, as well as negative self-image and dependency of others. According to Powell, the emotional issues and personality features may be enhanced by the brain damage and adaptation stress related to it (Powell 2005, p. 108). Utilizing music in rehabilitation settings may provide a holistic way considering the patient´s symptoms and emotional reactions, as well as a way for communicating and creating connections between the patient, close ones, care givers and new people, such as other patients.

Self-selected music may also provide support to the patient's identity and individuality as a person. According to Powell, depression following brain damage is often a good sign showing that the patient is conscious about the situation and its consequences (Powell 2005, p. 134-135). Ability to choose the musical environment may serve the emotional processing related to the situation. Moreover, the discussions about the reasons for choosing or not choosing certain music to listen to may provide a way for the close ones to understand how and if the patient is using music in dealing with the emotional challenges induced by the situation; is music used for comfort, escapism, or simply for entertainment. The change in habits related to music listening may also provide cues about emotional processing related to the recovery process.

4.3.4 Cognitive improvements induced by self-selected vocal music

According to the findings in the study of Sihvonen et al. daily listening of self-selected vocal music enhances cognitive rehabilitation after stroke more efficiently than listening to instrumental music or audiobooks, or only having standard care, especially for aphasic patients (Sihvonen et al., 2020). The self-selection of music adds to the individuality in rehabilitation, and the selected songs can be assumed to reflect patients´ personal taste in music.

Fischer et al. studied the effects of exposure to long known music with participants suffering from mild cognitive decline. Participants in this study selected

significant songs for daily listening. Based on the findings in this study the authors suggest that exposure to long known music may induce cognitive improvements and the effect might be even stronger for musicians compared with non-musicians. They also saw correlations between modest cognitive improvements and deactivation of related brain areas. The variety of music genres were chosen, but mainly vocal music. Based on this one may suggest that either vocal music is considered generally more significant, than instrumental, or the superior memory for vocal music plays a role when choosing for long known songs. (Fischer et al., 2021)

4.3.5 Neural activation induced by imagery singing of familiar songs

Listening to self-selected songs might also induce imagery singing, which has been related to increased activation of language areas Broca and Wernicke, on healthy participants (Gunji et al., 2007; Kleber et al., 2007). Based on these findings, imagery singing could be especially useful when aiming to support the recovery from language impairments. Imagery singing has also been found to increase activation on reward areas, such as nucleus accumbens, posterior cingulate, orbital cortex and parahippocampal gyrus, in comparison to speech (Callan et al., 2006).

In the rehabilitation process, the imagery singing could be supported with listening of familiar songs, listening to someone else sing familiar songs, or with participating into a choir, even if the voice production is compromised as a physical activity. The imagery of action as an effective method for neural stimulation is also supported by the well-known findings on the imagery movements activating the same brain regions as the conducted movements. The motivational aspect of self-selection in songs seems evident, but the overall significance of the familiarity-related neural activation on post-damage neural reorganization still calls for further investigation.

4.3.6 Emotional responses to music induced memories and aversive music

According to Garrido et al., song listening and musicking may reduce the need for pharmaceutical solutions for behavioral and psychological problems in care homes. However, familiar music may also induce negative memories and emotions, which should be considered when using music even if it was only played in the background (Garrido, Markwell, Andreallo & Hatcher, 2021). According to a recent study by Peltola & Vuoskoski, the reactions to unliked music may be neutral for some people, but for some they may include strong physical and psychological responses from muscle tension and physical pain to disgust and aggression (Peltola & Vuoskoski, 2022). Also, according to Peltola & Vuoskoski, the exposure to aversive music can induce perceived loss of agency and as a violation to moral, values and musical identity.

When using vocal music for behavioral and psychological issues such as depression it's also worth considering the findings and suggestions about automatic processing of lyrics (Gordon et al., 2010) and deeper semantic processing of lyrics in sad songs than in happy ones (Fiveash & Luck, 2016), especially when playing vocal music

on the background. The song that's comforting to some may be unmotivating or irritating to others and could provoke and enhance negative responses in patients who may have emotional and behavioral challenges to begin with, such as the emotional effects that are common after a brain injury mentioned in the previous chapter of this thesis. Based on the superior memory for vocal melodies (see Chpt 5.2) studied by e. g. Weiss et al. it could also be suggested that vocal melodies are most likely to induce memories of all kinds, because the participants recalled even the unliked vocal melodies better than the instrumental ones they liked (Weiss et al., 2015).

Based on these findings, the individuality in music taste and personal music experiences can significantly alter the behavioral and emotional responses to music listening and other musical activities. For instance, the seemingly sad songs may be experienced as comforting, while some of the seemingly happy songs could be related to and induce memories of traumatic events in the individual's life. The use of familiar songs should be considered as an effective way of activating neural networks if the potential responses and psychological and physiological side effects of music-related memories and experiences are kept in mind. Information about patient's musical experiences and music related habits before the brain injury could serve as a valuable background information for the rehabilitative use of music.

4.3.7 Musical autobiography as a tool for personalized rehabilitation methods

One of the tools for increasing understanding about individuality in music is through creating musical autobiography (MAB). According to Dassa (2018) creating a musical autobiography for elderly person can strengthen the sense of self-identity and illuminate their hidden facets, as well as provide occasions for mutual musicking and sharing experiences (Dassa, 2018). From rehabilitation point of view, the semantic associations and memories related to preferred songs and lyrics could be taken into consideration at least from a motivational point of view.

It calls for further investigation whether utilizing musical autobiography for singing interventions would affect the outcomes. Individual guidance in singing long known songs is not as easily arranged as an aphasia choir or personalized music listening. However, personalized musical support to the rehabilitation process could serve to increase patient's sense of agency and motivation to try harder, just as healthy people enjoy singing and listening to their favorite songs with lyrics they can relate to.

4.3.8 Summary

Based on the findings mentioned above, it's worth considering patient's musical preferences and reactions to aversive music when planning musical interventions for rehabilitation. Some people may have neutral reactions to aversive music, but in the worst-case scenario the unliked music induces strong physical or emotional responses that may affect the emotional environment in hospitals, care homes and homes. Music that´s irritating or passivating may also decrease the motivation of patient in

rehabilitation. It's also worth considering that the caregivers and the close ones of the patients are not immune to these effects of music. In therapeutic settings it may be necessary to encounter the negative emotions and memories also, but in neurological rehabilitation settings the motivational and activating effect of carefully, and individually, chosen music could support facing the challenges of hard tasks and re-learning of impaired skills.

Vocal music has often been chosen for self-selected listening, it seems to support cognitive rehabilitation, and the recall of vocal melodies is enhanced compared with instrumental. Based on these findings it can be assumed that s listening and singing of familiar songs activate our neural networks in an efficient way. The neural activation in listening to the liked songs is also altered based on the familiarity of songs.

For musicians, the listening of long known, significant songs seem to have an enhanced effect on cognitive rehabilitation, which may be based on the profound processing of the musical elements and semantics in lyrics. For background information, creating a musical autobiography could provide an access to the personal musical history of the patient, and to the memories and experiences that support the motivation and experience of agency in the rehabilitation process.

Same song could be passivating and boring to one patient, but highly motivating and inspiring to another. These individual differences in responses to music are a challenge for group interventions, but on the other hand, the group setting on its own can be a source of motivation for some. Singing group may be an easily accessible setting for an inexperienced singer to participate in, and in case where impairments in vocal production may not yet enable motor production of singing, imagery singing along may support the neural recovery.

Musical hobbies are usually goal-directed at some level, and there are individual differences in preferred forms of musicking; some people wish to sing on their own or with their voice teacher or a close one, some prefer singing in a band, group, or a choir, and some want to do both. These individual differences in preferences should be considered also when designing interventions and rehabilitative activities to support the recovery process.

The effects of personalized music interventions on neural reorganization should be investigated further. The motivational effect of music on physical exercise and neural rehabilitation is well-known, just as some neurological patients' capability to sing even when speech is impaired. However, it remains a topic for further investigation if the familiarity and liking of music has a direct effect on neural reorganization. The outcomes of preferred music listening may also be indirect, as the liking of music may result in repetitive listening, in which the repetition of the stimulus supports neural plasticity and reorganization.

The hypothesis 6 suggested that the musical autobiography, musical preferences and aims of music listening affect the reactions to vocal music in neurological rehabilitation. This was supported by findings showing that listening to self-selected music supports cognitive recovery. Individuality in responding to aversive music also

support the hypothesis, that reactions to music are affected by personal experiences. The effect of personal responses is also highlighted in the findings showing that familiarity affects the neural activation. Even when listening to preferred music only, the neural responses differ depending on the familiarity and novelty of music.

The emotional responses and challenges differ depending on the type and location on brain damage. The outcomes of brain damage may also alter how and why the patient chooses certain type of music to listen to. Listening of self-selected music has been found to support rehabilitation, but as a weakness there was no control group of patients who would've had randomized vocal music to listen to. However, considering the findings on responses to aversive music the study using regular exposure to randomized music for patients in vulnerable condition would have raised some serious ethical concerns. Further investigations should also be conducted for deeper understanding about the emotional effects and aims of music listening in neural rehabilitation.

5 DISCUSSION AND CONCLUSIONS

The aim of this thesis was to study neural activation and plasticity induced by singing and vocal music listening, combining findings on experience-dependent plasticity with outcomes of vocal music exposure in neural rehabilitation. Singing and vocal music listening activate the brain bilaterally, including auditory cortex, somatosensory cortex, front limbic areas and language areas Broca and Wernicke. However, in comparison to speech, neural correlates for singing and vocal music listening seems to be dominantly lateralized to the right hemisphere, and the right hemisphere activation has been suggested to underlie the enhancements of cognitive recovery induced by vocal music listening for patients with aphasia.

The right hemisphere activation in vocal music listening can be related to the activation of compensatory language areas, but it still calls for further investigation to find out how, and especially why, vocal music listening seems to support the recovery process. Moreover, to combine knowledge on the effects of learning and training of singing with the outcomes of singing related rehabilitation, the focus should also be on the impact of duration and repetition of stimuli.

According to the studies reviewed in this thesis, we have an enhanced recall for vocal music, unaffected by musical experience. Moreover, when participants were asked to choose significant music to listen to, most of it was vocal. The potential cultural differences weren't specifically addressed in these studies, but considering the findings, the emotional and associative effects of vocal music exposure shouldn't be ignored, even when the music is being played in the background. Both previous findings also support the suggestion, that musical interventions, especially the ones utilizing vocal music, should be personalized based not only on the symptoms or type of damage, but also on the musical autobiography of the patient. Neural responses to music differ based on the liking and familiarity of the music, and the semantic processing of lyrics may also vary depending on the individual responses and experiences. Familiar songs may also induce imagery singing and associative processing to support neural repair when motor functions of vocal production are compromised.

The integration between word and melody has been suggested to emerge instantly even for a single word. However, the semantics of the lyrics may not be processed neither instantly or automatically, and the process may be affected by the emotional experience induced by the music. Further investigations should be conducted to improve understanding about the semantic processing of lyrics. Vocal music interventions have been found to support neural recovery in case of aphasia, and the impairments in memory and speech production may not prevent singing familiar songs, but the significance of the semantics in lyrics for neural processes of musical memory and vocal production remains unclear.

Considering professionalism in singing, some of the main findings in this thesis were the experience-dependent plasticity changes in the structure and activation of insula and arcuate fasciculus. These structures have both been found crucial for language processing also, and the potential support that vocal music may provide to the recovery of these structures should be investigated in the context of neural rehabilitation.

Experience-dependent changes in arcuate fasciculus were found for both, instrumentalists, and singers, but the differences between these groups have begun to identify the specific effects of experience in singing. Longitudinal study on goal-directed singing training could improve understanding about the plasticity changes induced by the development of skill. Also, to fully understand the mechanisms leading to vocal expertise, the effects of physical training and emotion expression should be considered in further studies. In addition to studies on professional singers, the effects of singing training or extensive vocal music listening on neural plasticity should also be studied with adult hobbyists and beginners as participants, to be able to connect findings about experience-dependent plasticity to the potential of neural rehabilitation.

One of the goals for the current research was to identify needs for future investigations on the neuroscience of singing. This research has revealed several gaps in knowledge in relation to effects of singing and vocal music listening on neural plasticity. Four of these gaps are highlighted in the Table 5 with proposals for future studies. Table 5 also summaries the expected results and outlines their wider impact. (See Table 5)

TABLE 5: Gaps in knowledge and proposals for future investigations

Identified gap in knowledge	**Proposed study**	**Expected results**	**Wider impact**
The impact of music genre and sensitivity period on plasticity changes for professional singers	Comparison of structural changes and connectivity of insula and arcuate fasciculus on singers of different genres	GM volume decrease in insula correlates with the sensitivity period for the beginning of formal training. Later onset of training results in changes in white matter connections of insula and arcuate fasciculus	Neural correlates for singing different genres are understudied. The knowledge could be used to improve outcomes of voice education and neural rehabilitation utilizing vocal music.
The impact of regular training on neural plasticity on adult hobbyists of singing	Comparison of structural changes and connectivity of insula and arcuate fasciculus on hobbyist singers during the beginning of regular training	GM volume in insula is not affected by training. Activation of right insula increases. Increased volume in arcuate fasciculus correlates with language training.	The knowledge about neural activation induced by singing as a hobby could be utilized when developing singing interventions to support neural activation, and reorganization after brain damage.
Language processing during vocal music listening, and how it's affected by the increase of familiarity and musical memories	Comparison of the activation of language areas during listening of vocal music, audiobooks, or instrumental music on healthy people. Familiarity of songs is increased via repetitive listening.	Activation in the areas related to semantic processing of language, such as Wernicke, increases with repetition. Activation is greater for vocal music and audiobooks than for instrumental music	Knowledge about the semantic processing of lyrics could be used to develop music-based interventions for patients with impairments in speech comprehension. Increase of knowledge on the significance of lyrics and personal music history.

Short-term and long-term effects of singing on neural plasticity	Comparison of the plasticity changes induced by short term training for hobbyists and long-term training of professional singers.	Neural activation perceived in short-term training of singing is strengthened for professional singers. Outcomes are affected by the timing of onset of formal training and by the familiarity of music genre being trained.	Findings of this study would provide increased knowledge about the impact of timing and duration of singing training on neural organization. Knowledge could be used for assessment of effective duration for singing education and interventions.

The main challenge in the assessment of the findings in this mapping review emerged from the fragmentation of knowledge. Participant number in the studies concerning neural rehabilitation was often relatively small, and the details about the neural plasticity effects of vocal music listening on neural reorganization remain unclear. It also calls for further investigation to study how language processing in vocal music listening affects neural plasticity, or if the role of music listening is a background activity that enhances spontaneous recovery. Conditions of care may also affect the accessibility of rehabilitation in general. Further research could increase knowledge on how the emotional state and personality features could affect the self-selection of vocal music, and how these individual features may affect the neural plasticity induced by musical stimuli.

When considering the expected outcomes of music-related rehabilitation methods, the emotional outcomes of music exposure should be taken under consideration. Responses to music may alter from joy and comfort to neutral, but also to strongly negative reactions from feelings of disgust to violation of musical identity. Based on these findings, ignoring the individuality in music experiences and responses could affect negatively on the patient's experience and motivation already during the otherwise well-designed interventions. It also calls for further investigation if and how the emotional responses affect the neural reorganization.

There were some limits also to the reviewed studies considering experience-dependent plasticity. Suggested sensitivity period at around age of 14 in the beginning of formal training was related to opera singing, and it calls for further investigation how later onset of formal training or training of different music genres would alter the effects on plasticity. One of the differences between some other genres and classical singing is the extensive variety of languages utilized in the latter one, suggesting some experience-dependent plasticity related to lingual experience. Moreover, the genre-

related differences in the physical and interpretative demands of different genres may also affect the location and strength of neural activation, as well as the connectivity of the associative network. Neural responses to different genres may be affected by the musical features of the genre, but also by the experience-dependent plasticity related to the musical background of the person involved.

To expand background research for the development of vocal music interventions from this thesis further, studies on music and motivation also provide knowledge on the self-selection of music. Studies reviewed here focused on the production of singing and the processing of auditory stimuli in vocal music listening but review of the findings on visual processing of singing could also provide directions for future investigations. The potential plasticity effects of movement or observation of movement during singing or vocal music listening should also be investigated further to identify the effects of mirroring and interaction.

The value of this research arises from the increase of knowledge on the neural processing of vocal music. Previous studies have addressed singing and vocal music related plasticity related to professionalism and neural rehabilitation. This thesis provides a framework to consider rehabilitation as a process of learning and relearning and suggests that the efficiency of vocal music rehabilitation could be improved based on the knowledge of the neural effects of experience in singing. The knowledge gained from this research arises from the multidisciplinary approach that combines the effects of exposure, expertise, and individual experience to identify the potential and limitations of vocal music induced neural plasticity.

Weakness of this review is that it cannot provide any new findings from brain imaging, cognitive tests, or interviews. The research process revealed more questions than answers. However, this thesis provides a basis for future investigations by combining existing knowledge, shedding some light to the limitations of the existing studies, and identifying gaps in knowledge. Based on the findings in this research the neural rehabilitation methods can be personalized according to individual music experiences and responses to vocal music.

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