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Singing for rehabilitation: Efficacy of singing-based interventions in major ageing-related neurological disorders

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Abstract

For the human brain, singing is versatile form of communication that engages a large-scale bilateral network of temporal, frontal, parietal, cerebellar, and limbic networks associated with auditory, linguistic, speech-motor, cognitive, emotional, and social processes. In ageing-related neurological disorders affecting verbal communication, vocal-motor functions, and memory, singing can be highly rewarding, fun, and motivating and can provide a valuable tool for enhancing verbal and emotional expression, cognition, and social interaction. This Chapter summarizes recent advances in uncovering the neural basis of singing and reviews the current evidence on the clinical efficacy of singing-based interventions in the rehabilitation of the most common, and severe, ageing-related neurological disorders: aphasia, Alzheimer's disease, and Parkinson's disease.

Keywords: singing, rehabilitation, aphasia, Alzheimer's disease, Parkinson's disease

"Where words fail, music speaks." This famous quotation from the Danish writer and poet Hans Christian Andersen (1805 – 1875) highlights one of the most fundamental aspects of music: its ability to convey and express emotions, and to communicate and share meaningful experiences with others. While this holds true for all of us, the emotional and communicative power of singing and music is particularly evident in persons with neurological illnesses affecting verbal expression, vocal-motor control, and memory.

In general, music is an important source of enjoyment, learning, and well-being across life, as well as a rich, powerful, and versatile stimulus for the brain. With the advance of modern neuroimaging techniques during the past decades, we now have a much better grasp of the neural underpinnings of music and singing and of the neuroplasticity mechanisms underlying the motor, cognitive, and verbal gains induced by musical training in the healthy brain. This knowledge is crucial for understanding how music, particularly singing, could be effectively utilized also as a neurological rehabilitation tool (Sihvonen et al., 2017a).

This Chapter aims to provide an overview of the key brain networks that govern the processing of music and singing in the healthy brain and to present recent findings on the rehabilitative efficacy of singing in three neurological disorders: post-stroke aphasia, Alzheimer's disease (AD), and Parkinson's disease (PD).

Neural basis of singing in the healthy brain

The ability to perceive, enjoy, and produce music is a fundamentally human feature, present across cultures and developing very early in life. For the human brain, music arguably ranks among the most complex and penetrative stimuli, engaging a large-scale bilateral network of temporal, frontal, parietal, cerebellar, and limbic and paralimbic brain areas associated with cognitive, verbal, motor, and emotional processes.

Brain networks underlying music perception in the healthy brain

Figure 1 summarizes the different neural networks engaged by the perception, experience, and production of music. The *basic auditory features* of music (i.e., spectral and temporal variation) are encoded and analyzed along the ascending auditory pathway, carrying sound information from the inner ear to the brain stem and the thalamus, and projecting from there to the auditory cortex in the superior (upper) part of the temporal lobe (Zatorre, Belin, & Penhune, 2002). After this initial perceptual encoding stage, music processing unfolds over multiple spatially distributed networks governing higher-level perceptual, cognitive, motor, and emotional functions. *Higher-order musical features* (e.g., chords, melody) are processed by a network comprising inferior (lower) and medial (towards the middle) prefrontal areas, premotor areas, anterior (toward the front) and posterior (toward the back) superior temporal areas, and inferior parietal areas (Janata et al., 2002; Patel, 2003). The *periodic rhythm (beat)* of music as well as the motor production of music (e.g., instrument playing, tapping to beat) is further accomplished by a network of motor regions in the frontal motor and premotor cortices, basal ganglia, and cerebellum (Grahn & Rowe, 2009; Zatorre, Chen, & Penhune, 2007). The *attention and working memory* system in the inferior and dorsolateral (upper and towards the side) prefrontal cortex, cingulate cortex, and inferior parietal cortex is recruited to focus our attention to music as it unfolds over time (Janata, Tillmann, & Bharucha, 2002; Jerde, Childs, Handy, Nagode, & Pardo, 2011).

Figure 1. Key brain regions associated with the processing of music overlaid with the main singing-related pathways based on fMRI and PET studies of healthy subjects. Note: Although the figure displays the right hemisphere, most of the music processing networks are largely bilateral. ACC = anterior cingulate cortex, aINS = anterior insula, dPMC = dorsal premotor cortex, IFG = inferior frontal gyrus, IPS = intraparietal sulcus, STG/STS = superior temporal gyrus/sulcus. Adapted from Särkämö and Sihvonen (2018).

Recalling long-term memories associated with music engages the *episodic memory system*, which covers many areas in medial temporal (e.g., hippocampus), parietal (precuneus, angular gyrus), and frontal [dorsomedial (upper and towards the middle) and inferior prefrontal] lobe (Janata, 2009; Platel, Baron, Desgranges, Bernard, & Eustache, 2003). Finally, the affective impact of music and the hedonic pleasure derived from music is closely linked to the dopaminergic *emotion and reward network* of the brain, involving midbrain structures, the nucleus accumbens of basal ganglia, the amygdala, the hippocampus, the cingulate cortex, and the orbitofrontal cortex (Koelsch, 2014; Zatorre & Salimpoor, 2013).

Brain networks underlying song perception and singing in the healthy brain

Neuroimaging studies in healthy subjects have shown that music and speech share processing resources in many parts of the brain, including temporal, frontal, and parietal areas. However, they also engage distinct cortical networks (LaCroix, Diaz, & Rogalsky, 2015). Results from recent fMRI pattern analysis studies, which have directly compared natural speech and music processing in the same subjects, indicate that, while speech and music both engage bilateral (both left and right hemisphere) superior temporal areas extensively, speech is processed more ventrolaterally (lower and towards the side), and music more dorsomedially (Norman-Haignere, Kanwisher, & McDermott, 2015; Rogalsky, Rong, Saberi, & Hickok, 2011). This suggests distinct spatial patterns and stages of processing for speech and music within the same temporal network.

Conceptually, **songs** represent an interesting interface between speech and music, binding lyrics and melody into a unified representation. Thus, the neural processing of songs is a combination of linguistic (syntactic, semantic), musical (melodic, rhythmic), domain-general cognitive (attention, memory), vocal-motor, and emotional processing. Evidence from fMRI studies suggests that listening to singing activates bilateral temporal (e.g., superior temporal gyrus, planum temporale) and frontal (e.g., superior frontal gyrus, premotor cortex) areas as well as subcortical / limbic areas (e.g., hippocampus, striatum, orbitofrontal cortex) more extensively than listening to speech (Callan et al., 2006; Schön et al., 2010) or instrumental music (Alluri et al., 2013; Brattico et al., 2011). This suggests that the perception of singing engenders stronger and more wide-spread auditory, linguistic, and emotional processing in the brain than speech or music alone. The perception of vocal melodies also engages the right sensorimotor cortex and its connectivity with other parts of the auditory dorsal stream, a key pathway of audio-vocal integration in speech production (Lévêque and Schön, 2015).

The **production of singing** entails continuous interaction between two cortical systems, the dorsal (upper) parietal-frontal vocal production pathway and the ventral (lower) temporal-frontal auditory perception pathway (see Figure 1), coupled with the engagement of abovementioned wide-scale language and music processing networks (Brown, Martinez, Hodges, Fox, & Parsons, 2004; Callan et al., 2006; Özdemir, Norton, & Schlaug, 2006; Kleber, Veit, Birbaumer, Gruzeliér, & Lotze, 2010; Zarate, 2013). Compared to speaking, singing activates bilateral (although stronger in right than left) superior temporal areas, pre- and post-central gyri, and inferior frontal areas more extensively (Brown et al., 2004; Callan et al., 2006; Özdemir et al., 2006). This has major clinical implications for aphasia rehabilitation.

Preservation and efficacy of singing in neurological disorders

Singing and aphasia

The notion that even severely aphasic stroke patients, who are unable to produce speech, can retain the ability to sing lyrics of familiar songs is one of the classic observations in neurology, dating back to 1740s (Johnson & Graziano, 2015). However, experimental evidence for this is surprisingly scarce and mixed. Some case studies and small group studies in aphasics report better singing vs. speaking of familiar song lyrics (Hébert, Racette, Gagnon, & Peretz, 2003; Jacome, 1984; Straube, Schulz, Geipel, Mentzel, & Miltner, 2008; Yamadori, Osumi, Masuhara, & Okubo, 1977) and some do not (Prior, Kinsella, & Giese, 1991; Racette, Bard, & Peretz, 2006). In an fMRI study exploring activation patterns evoked by passive listening to natural vocal (sung) and instrumental, familiar song excerpts in 41 stroke patients, preserved processing of vocal music was seen in the right superior and middle temporal areas in aphasic patients (Sihvonen et al., 2007b).

Aphasics are able to repeat words with the help of a sung auditory model (Racette et al., 2006), and singing is a highly promising tool in aphasia rehabilitation. It can train speech-motor difficulties at many levels, for example by slowing production rate, increasing connectedness between syllables and words, and using melody as a retrieval cue for words and rhythm to facilitate sound-motor mapping (Wan, Rüber, Hohmann, Schlaug, 2010). In *Melodic intonation therapy* (MIT), speech production is trained by melodically intoning common phrases at slow pace coupled with left hand-tapping, following a hierarchy of steps that progress from singing to speech. Studies in Broca's aphasics (aphasic patients who have difficulty speaking fluently whereas their comprehension is relatively preserved) have reported beneficial effects of MIT on connected speech, naming, and repetition (Sparks, Helm, & Albert, 1974; Zumbansen, Peretz, & Hébert, 2014; van der Meulen, van de Sandt-Koenderman, Heijenbrok-Kal, Visch-Brink, & Ribbers, 2014). In neuroimaging studies, the positive effect of MIT in aphasia has been linked to increased activation, or neural processing efficiency, in speech production in temporal and frontal speech-motor areas, both in the left hemisphere (Belin et al., 1996; Breier, Randle, Maher, & Papanicolaou, 2010) and in the right hemisphere (Schlaug, Marchina, & Norton, 2008; Wan, Zheng, Marchina, Norton, & Schlaug, 2014; Tabei et al., 2016).

In addition to aphasia, singing-based interventions have been used in **dysarthria**, a common motor speech disorder after stroke, with two case studies reporting benefits in speech motor coordination (e.g., respiration and articulation) and prosody (Kim & Jo, 2013) and in speech intelligibility and naturalness (Tamplin, 2008).

Listening to music can have a rehabilitative effect during the early stages of stroke recovery. Särkämö and colleagues performed a parallel-group RCT comparing the long-term effects of a 2-month daily music listening (min 1 hour per day) intervention to an audio book listening intervention and standard care (control group) in acute stroke patients (N = 60) (Forsblom, Särkämö, Laitinen, & Tervaniemi, 2010; Särkämö et al., 2008, 2010, 2014a). Both the audio book and music material were self-selected and the listening was self-administered using portable players, with the support of music therapists, family members, and nursing staff. The music comprised mostly songs with lyrics that were familiar to and preferred by the patients. In a 6-month follow-up, music listening was found to be superior to audio book listening and standard care in improving the recovery of verbal memory and focused attention and reducing depression and confusion (Särkämö et al., 2008) as well as in increasing positive mood, relaxation, and motor activity (Forsblom et al., 2010). Using magnetoencephalography (MEG), these behavioural gains induced by music listening were also linked functionally to enhanced neural efficiency of auditory encoding, as indexed by stronger mismatch negativity (MMN) responses (Särkämö et al., 2010). Using voxel-based morphometry (VBM) analyses of structural magnetic resonance imaging (sMRI) data, music listening was also

found to enhance structural neuroplasticity as indicated by increased grey matter volume in spared prefrontal (superior frontal gyrus) and limbic (anterior cingulate, ventral striatum) regions in left hemisphere-lesioned patients (Särkämö et al., 2014a).

Recently, there has been increasing interest in group-based music interventions, which have the added value of being more widely applicable and involving a social interaction element compared to individual-based methods. The effects of *choral singing* have been explored in three small pilot studies. Qualitatively, participating in a community choir is perceived by stroke and Parkinson's disease patients as helpful in the self-management of the social and emotional consequences caused by the illness, such as social isolation, low mood, and communication deficits (Fogg-Rogers et al., 2016). In a within-subjects questionnaire and interview study by Tamplin and colleagues (Tamplin, Baker, Jones, Way, & Lee, 2013), aphasic stroke patients (N = 13) reported reduced psychological distress and enhanced confidence, mood, motivation, and communication after participating weekly in a community choir for 20 weeks. Recently, in a pilot, three-arm RCT of chronic aphasic patients (N = 23), Zumbansen et al. (2016) compared the effects of weekly choir and drama group interventions to standard care. While no significant outcome effects were observed for the interventions, the level of attendance at the social activities was linked to improved functional communication, and the protocol was found to be feasible.

Singing and dementia

Music-induced emotions and memories are often preserved in persons with dementia (PWD), even in more advanced stages (Cuddy, Sikka, & Vanstone, 2015). This is possibly due to relative preservation of medial frontal and limbic areas in people with Alzheimer's Disease (AD) (Jacobsen et al., 2015). Persons with AD have been reported to be able to also recognize lyrics of novel songs when presented in sung format (Moussard, Bigand, Belleville, & Peretz, 2014; Simmons-Stern, Budson, & Ally, 2010) and also to be able to learn a novel song (Baird, Umbach, & Thompson, 2017). Engagement in musical activities, such as listening to music or singing along to songs, appears to be natural for persons with AD; in some cases, it can even increase after the onset of AD, regardless of disease severity (Midorikawa et al., 2016). Overall, music appears to be important for PWDs as a means of providing enjoyment and improving mood, maintaining personal identity, and facilitating social interaction and connectedness in the care environment (McDermott, Orrell, & Ridder, 2014).

The majority of music-based intervention studies in dementia have focused on PWDs with moderate-severe dementia and have utilized either music listening or a combination of listening, singing, and instrument playing in the context of music therapy. Overall, the results of randomized controlled trials (RCTs) on these interventions have been mixed, some showing positive effects on neuropsychiatric symptoms, such as agitation, anxiety, and depression (Guétin et al., 2009; Lin et al., 2011; Ridder, Stige, Qvale, & Gold, 2013) and others showing no significant effects (Cooke, Moyle, Shum, Harrison, & Murfield, 2010; Narme et al., 2014; Raglio et al., 2015; Vink et al., 2013). The quality of evidence is currently moderate for the efficacy of music therapy on depression and agitation but low for other domains, such as cognition, quality of life, and social behavior targeted by the intervention (van der Steen et al., 2017).

In addition to music intervention studies in more advanced dementia, there has recently been interest in the efficacy of music in the earlier stages of dementia. Särkämö and colleagues (Särkämö et al., 2014b, 2016a, 2016b) conducted a parallel-group RCT in PWDs with mild-moderate dementia (N = 89) and their caregivers (family members and nurses) comparing the short- and long-term efficacy of two 10-week music interventions to standard care. The interventions comprised both group sessions and home training, which focused on coaching the caregivers of PWDs to use either regular singing or listening of familiar songs together with the PWD at home or care unit. Both singing and music

listening were found to help maintain general cognition, as indicated by higher scores on Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and executive function, enhance remote episodic memory, and alleviate depression (Särkämö et al., 2014b). As shown in Figure 2, singing was particularly effective in enhancing verbal working memory, especially in PWDs who had mild dementia, as well as in reducing the psychological stress and burden experienced by the caregivers (Särkämö et al., 2014b, 2016a). The positive effects of music on depression were also more prominent in PWDs with mild AD-type dementia (Särkämö et al., 2016a), and there was a partly different pattern of emotional benefits in the two music interventions: music listening was more calming and relaxing (reducing agitation) whereas singing was more energizing and refreshing (reducing fatigue) compared to standard care (Särkämö et al., 2016b).

Figure 2. Positive changes (mean $\pm$ SEM) in verbal working memory and caregiver burden in PWDs after a 10-week singing intervention compared to a music listening intervention and standard care. Both short-term (from baseline [BL] to immediate post-intervention follow-up 1 [FU1]) and long-term (from BL to 6-month post-intervention follow-up 2 [FU2]) are shown. Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$ by mixed-model ANOVA (Time $\times$ Group interaction). Adapted from Särkämö et al. (2014b), Särkämö et al. (2016a).

Regarding the cognitive effects of singing, convergent results have recently been obtained in two cohort studies. Maguire and others reported that 4 months of regular group singing, but not music listening, improved performance on tests of general cognition and visuospatial processing in PWDs ($N = 45$; Maguire, Wanschura, Battaglia, Howell, & Flinn, 2015). Similarly, Satoh et al. (2015) found that psychomotor speed and mood were improved in PWDs ($N = 10$) after a 6-month karaoke-based singing training program. Interestingly, these effects were coupled with decreased parietal activation in an fMRI karaoke task, suggestive of improved neural efficiency of cognitive processing (Satoh et al., 2015). A recent study by Dassa and Amir (2016) looked at conversational patterns in a small group ($N = 6$) of PWDs during and after group sessions involving singing familiar songs. They

observed that singing led to extensive and spontaneous conversation about the memories evoked by songs, with PWDs also expressing positive feelings and a sense of belonging.

Further evidence concerning the social aspects of singing comes from a dyadic study of PWDs and their family carers (N = 10) participating in group singing together (Camic, Williams, & Meeten, 2013). The study found no significant effects of singing on standardized measures of cognition, mood, and QOL, whereas engagement levels were very high and qualitative data showed strong positive effects on wellbeing (Camic et al., 2013). A similar, qualitative study (Unadkat, Camic, & Vella-Burrows, 2017) of PWD-caregiver couples (N = 17) also found that, while PWDs and caregivers benefitted from the singing activity independently (e.g., supporting identity and confidence in PWDs and providing enjoyment and liberation in caregivers), the activity also had a positive, relational impact for them as a couple (e.g., enhancing togetherness). Experiences from the popular Singing for the Brain™ program, an intervention based on group singing activities developed by the Alzheimer's Society UK for PWDs and their carers, have also been positive, with participants reporting positive effects on social relationships, memory, and mood as well as on acceptance of dementia and coping with it in daily life (Osman, Tischler, & Schneider, 2016).

Singing and Parkinson's disease

Gait impairment, including reduced speed, cadence, and stride length, are among the key motor symptoms of Parkinson's disease (PD), and the majority of the music-based intervention studies in PD have been targeted towards enhancing gait through external auditory stimulation provided by the rhythm of music or metronome beat (for recent reviews, see Ginis, Nackaerts, Nieuwboer, & Heremans, 2017; Shanahan, Morris, Bhriain, Saunders, & Clifford, 2015; Sihvonen et al., 2017). Recently, two studies explored whether the rhythmic benefits of music extended also to vocal-motor behavior in PD. Harris, Leenders, and de Jong (2016) compared persons with Parkinson's disease (PwPD, N = 15) to healthy controls in spontaneous speech production and in singing of familiar and improvised melodies. Compared to healthy controls, the PwPDs exhibited impairments of expressive prosody in speech whereas their singing was unimpaired as indicated by both perceptual and acoustic analysis. In a within-subjects study of 23 PwPDs, Harrison, McNeely, and Earhart (2017) compared gait patterns in five cueing conditions: uncued, music only, singing only, singing with music, and verbal dual-task. Singing only had the best positive effect on gait variability with no detrimental effects on velocity, cadence, or stride length, suggesting that self-generated singing is a promising cueing technique in PD.

Many PwPDs also suffer from disorders of speech, such weak or hoarse voice, imprecise articulation, or impaired stress or rhythm in speech. In within-subjects intervention studies (N = 4-28), singing-based interventions have been reported beneficial in PwPDs for enhancing speech production with regards to speech prosody, vocal fatigue, and phonation as well as and intelligibility and intensity of speech (Di Benedetto et al., 2009; Haneishi, 2001; Evans, Canavan, Foy, Langford, & Proctor, 2012; Tanner, Rammage, & Liu, 2015). Although these findings are promising, further research is still required to ascertain these effects using larger studies with RCT designs. More research is also needed to assess potential wider benefits of singing on communication, cognitive-motor functions, and quality of life in PD (Barnish, Atkinson, Barran, & Barnish, 2016).

Concluding remarks

In summary, based on the studies reviewed above, there is now emerging evidence that singing is an extremely versatile and pervasive activity for the human brain, enlisting a highly wide-scale bilateral network of temporal, frontal, parietal, cerebellar, and limbic regions. Evidence from clinical

behavioural studies suggests that singing is a very promising tool in neurological rehabilitation. Singing be used to train speech production in aphasia, memory and cognitive functioning in AD (at least in the early stages of the illness), and also vocal-motor functioning in PD. In addition to these specific domains, singing naturally has generic benefits for emotional adjustment, mood, and social interaction, which seem to be common in all neurological disorders. Group-based singing interventions, such as choral singing programs tailored for specific patient groups, hold much promise as cost-effective and easily scalable interventions.

Overall, although positive findings from individual studies are converging to support the use of singing in neurological care and rehabilitation, large and high-quality RCTs are still needed to build a more solid clinical evidence base and to establish the use of singing more widely in the rehabilitation and care units. Especially singing intervention studies focusing on the very early, prodromal stage of dementia (subjective memory impairment / mild cognitive impairment stage) and including a long (many years) follow-up period would be important to determine the potential of singing in slowing neurocognitive decline at the onset of the first signs of memory impairment. In this vein, establishing the “dose-response” of singing over a long time period would be pivotal in determining how long and frequent should singing sessions be to achieve optimal longitudinal gains. Moreover, structural and functional neuroimaging studies in patient populations are also needed to gain a deeper insight about the impact of different neuropathologies on singing-related auditory perceptual and vocal-motor skills as well as on potential neuroplasticity processes induced by singing-based rehabilitation in different neurological disorders. This information is pivotal in elucidating the neural mechanisms underlying the efficacy singing and, eventually, in helping to better target singing interventions at the individual level for different neurological disorders.

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