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Music Cognition in Breast Cancer Survivors

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Abstract

Advances in breast cancer treatment have resulted in improved survival rates and concomitant reports of chemotherapy-related cognitive dysfunction. Music cognition, a form of general cognition, also may be negatively affected by chemotherapy. Moreover, chemotherapy may have general ototoxic effects. The goal of this study was to explore whether breast cancer survivors (BCS) had similar hearing thresholds and music cognition abilities compared with age-matched healthy controls (HC). A total of 56 women (28 BCS and 28 HC) completed the audiometric tests and the Montreal Battery Evaluation of Amusia (MBEA). Results indicate the 2 groups have similar hearing thresholds. A comparison of music cognition variables suggests possible differences in some music cognition tasks, with HC scoring slightly, but not significantly, better in melodic perception. The BCS scored slightly better, though not significantly, on melodic memory. An adequately powered study including cognitive variables is needed for verification of findings and to establish clinical meaningfulness.

Keywords

breast cancer survivors, music perception, chemotherapy, cognitive dysfunction, hearing loss

Review of Literature

Breast cancer is the most common form of cancer among women, accounting for 28% of all cancers.[1] Advances in treatment have resulted in a relatively high survival rate across all types of breast cancers (eg, about 90% [localized and regional]), regardless of patient age.[2] Given the high frequency of breast cancer and advances in treatment, any residual problems associated with breast cancer or its treatment are likely to affect large numbers of women.

Up to 83% of breast cancer survivors (BCS) report some form of cognitive dysfunction after chemotherapy.[3-6] Neuropsychological studies support complaints about declines in cognitive function.[6,7] For example, meta-analysis reveals that BCS, as a group, showed lower performance on objective tests of cognitive function compared with healthy controls (HC).[8] The most frequently affected cognitive domains include verbal memory capacity, executive functioning, and psychomotor speed, with clinically significant impairment occurring in 15% to 25% of BCS.[9]

Music cognition is a special case of general cognition involving multiple mechanical, chemical, and neural activations beginning with the hearing mechanism and ending with cognitive interpretation. Aside from the hearing mechanism, music cognition involves a complex array of perceptual analyses of the auditory signal. Music listening, for example, includes focus of attention, rapid serial encoding of notes (and words), and recognition and identification of these patterns as familiar songs via melodic and temporal organizations.[10]

Melodic (pitch contour, intervals, and tonality) and temporal (meter and rhythm) organizations provide valuable information about communicative meaning such as emotion, irony, and humor, and may provide syntactic segmentation cues to listeners. Melodic and temporal organizations are often conceptualized as 2 distinct processes.[8,11] Deficits in the perception of melodic contour (higher or lower pitch) may have a cascading effect on the perception of pitch intervals (melodic steps or skips) and tonality (musical scale systems). Similarly, deficits in perceiving meter may have an effect on perception of rhythm and vice versa. These domains often are considered

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independent, but deficits in perception of both melodic and temporal features can result in impaired melody recognition.[10]

Recent research has demonstrated significant correlations between performance on music cognition tasks and working memory, learning, executive functioning, and mental flexibility skills.[4] In fact, music training has been linked to the development of perceptual and neurocognitive skills, such as understanding speech in noise,[12,13] processing prosody and emotional vocal sounds,[14-16] processing linguistic pitch,[17] verbal and auditory memory,[18-21] executive functioning,[22-24] and even gains in intelligence quotient (IQ).[25] These effects may be due to changes in structural and functional brain development resulting from active music experiences.[26-29] Finally, some studies have reported a positive correlation between melodic organization skills and performance on speech perception tasks in normal-hearing and hearing-impaired listeners.[30,31]

Since music perception and cognition are a component of general cognitive abilities, negative changes due to chemotherapy might be associated with deficits in music cognition skills as well as basic cognitive processing abilities. Therefore, determining whether adjuvant breast cancer treatment results in general auditory and music perception deficits is essential in order to shape best-practice models for music-based interventions in oncology. On a more general level, chemotherapy may have ototoxic effects in patients with cancer. To that end, the overall goal of this pilot study was to explore whether BCS who have received adjuvant cancer treatment have similar hearing thresholds and music perception and cognition skills compared with healthy age-matched controls.

Methods

Study Sample

Participants included 28 female BCS and 28 HC who participated in the Mechanisms of Human Cognitive Dysfunction ([MHCD] F. Unverzagt PI) study. The BCS were recruited from a cancer registry, local breast cancer support groups, cancer centers/clinics, hospitals, churches, community centers, and other organizations. Recruitment advertising included an informational flier, press release, and oral presentation describing the purpose and procedures of the study for these participating organizations. Inclusion criteria for BCS were (1) self-reported history of breast cancer, (2) self-reported history of chemotherapy treatment for breast cancer, (3) living independently in the community, (4) absence of self-reported major psychiatric disorder (major depression, bipolar disorder, history of schizophrenia, or psychosis from any cause) or neurologic condition (learning disability, head injury with loss of consciousness greater than 60 minutes, epilepsy, stroke, brain tumor, brain infection, or brain degeneration), and (5) 40 years of age and older. The average time since diagnosis for BCS was 7.16 years (standard deviation [SD] = 2.91), with a majority of women (57%) diagnosed at tumor stage I or II.

The HC were recruited from a research registry, nominations from enrolled BCS, and advertisements posted at local churches and community centers. Inclusion criteria for HC were identical to those for the BCS other than absent self-reported history of any cancer (other than skin cancer) or treatment with chemotherapeutic agents for any reason. The HC were matched to enrolled BCS by age ($\pm$5 years) and education ($\pm$3 years). In all, 25 (89%) of the HC participants and 100% of the BCS participants reported being postmenopausal.

Setting

Testing took place at the DeVault Otologic Research Laboratory located in the Research Wing of the James Whitcomb Riley Hospital for Children. The laboratory included a sound-treated testing booth with observation facilities.

Stimuli and Procedures

Music listening/preference survey. It is a series of questions developed for this study regarding participants' music background (eg, years of music lessons and current musical involvement), music preferences, and music listening habits. The BCS were also asked to indicate the degree of pre- to postchemotherapy change in their music listening habits, enjoyment of music, music preferences, and emotional response to music.

Pure tone average. Hearing thresholds were measured via headphones with pure tones at frequencies ranging from 250 to 6000 Hz bilaterally. Hearing levels (HL) are expressed in decibels (dB) and labeled by severity: normal hearing (−10 to 15 dB HL), slight (16-25 dB), mild (26-40 dB), moderate (41-55 dB), moderately severe (56-70 dB), severe (71-90 dB HL), and profound hearing loss (91 dB or greater).[32] Pure tone average (PTA) is calculated by averaging the hearing thresholds across frequencies and ears. A change of 10 to 15 dB at any frequency is clinically significant.

Music cognition. The Montreal Battery Evaluation of Amusia (MBEA) contains 6 tasks that test auditory skills ranging from melodic contour perception to melody recognition (described below).[11] All 6 tasks use the same 30 musical phrases composed to follow traditional Western tonal systems. Phrases last from 3.8 to 6.4 seconds in all but the meter test, which is twice as long (average 11 seconds). We calculated individual task scores as well as an average from all 6 tasks.

Contour, intervals, and tonality (melodic organization). In the melodic organization tasks, participants were presented with a target melody and then asked to determine whether the comparison melody was the same or different. The melodies were manipulated in one of the following three ways: (1) the contour manipulation involved modifying the pitch of a critical note so that there is a change in pitch direction (eg, a series of notes change from an up-down-up contour to a down-up-up contour), without influencing the tonality, (2) the interval manipulation involved modifying the pitch of a critical note, resulting in a change in the size of the pitch interval (eg, 5 semitones vs 7 semitones), without changing the melodic contour, and (3) the tonality was manipulated by changing the pitch of a note so that it was out of the established key, while maintaining the melodic contour.

Rhythm and meter (temporal organization). In the temporal organization tasks participants were again presented with a target melody and asked to determine whether the comparison melody was the same or different. In the rhythm perception task, participants were presented with pairs of melodies, which were the same or differed by a small durational change on one of the notes. Such a change may disrupt the sense of a continuous "beat" in the melodic passage. The meter task required the participant to categorize melodies as a waltz (3 beats per measure) or a march (4 beats per measure).

Musical memory. There were 2 types of tasks intended to measure memory of melodies. Participants listened to individual melodies and determined whether they recognized the melody. The 3 types of stimuli were (1) old-old, consisting of 20 standard familiar tunes. Half of these tunes are typically learned with lyrics (eg, "Happy Birthday") and half are learned without lyrics (eg, Gershwin's "Rhapsody in Blue"). These 2 types of tunes were used to determine whether perception of melodies was moderated by linguistic content, (2) old, consisting of 10 melodies participants heard for the first time in the previous pitch and rhythm perception tasks, (3) new, consisting of 10 melodies participants never heard before. Melodies in all 3 conditions were performed without accompanying harmonies. Participants completed the memory test after the hearing, melodic, and temporal organization tests.

The Indiana University–Purdue University in Indianapolis (IUPUI) Behavioral Institutional Review Board approved this study and the participants completed the required authorization and consent forms prior to testing. All participants received audiometric tests first and the music cognition tests at last. Trained research assistants conducted the audiometric testing and the music cognition battery was automated via computer. Participants completed the music listening/preference survey prior to testing. Testing lasted approximately 75 minutes. Participants were compensated $20 for completing the testing.

Statistical Methods

The BCS and HC groups were compared on demographic and clinical variables using McNemar test for categorical data and paired t tests for continuous data. The BCS and HC were compared with a normative group using unequal variance t tests. To estimate the correlation between hearing and melodic organization and compare BCS with HC participants on music cognition variables, we used linear mixed models, which took into account the matching of HC to BCS participants. The PTA was included in the models as a covariate. The significance level was set at .05. All analyses were performed using SAS Version 9.2 (Cary, North Carolina).

Table 1. Sample Characteristics

	BCS (n = 28)		HC (n = 28)		*P* Value (2-Tailed)
	Mean	SD	Mean	SD	
PTA	16.9	10.3	19.9	10.8	0.11
Age, y	59.5	10.6	60.4	9.6	0.13
Education, y	15.5	2.1	15.9	2.4	0.34
	Count	%	Count	%	
Race					
White	26	92.9	25	89.3	0.66
Other	2	7.1	3	10.7	
Marital status					
Married	21	75.0	19	67.9	0.53
Nonmarried	7	25.0	9	32.1	
Music training					
Yes	21	75.0	20	71.4	0.78
No	7	25.0	8	28.6	

Abbreviations: BCS, breast cancer survivors; HC, healthy controls; PTA, pure tone average; SD, standard deviation.

Results

Results indicated that the groups (BCS and HC) are similar in hearing thresholds and music training (see Table 1). The 3 most common BCS chemotherapy treatment combinations received were adriamyacian/cytoxan (39%), taxol/adriamyacian/cytoxan (14%), and adriamyacin/taxotere (11%). In all, 25 (44.6%) of the women had normal hearing, 30 (53.6%) had slight to mild hearing loss, and one woman (1.8%) had moderate hearing loss. There was a significant, moderate, negative correlation ($r = -.34$, $P = .001$) between hearing thresholds and scores on the 3 melodic organization tests across all participants. There was no correlation between hearing thresholds and scores on the temporal organization tests.

Responses to the music listening/preference survey indicated that very few women experienced changes in music listening habits or listening preferences after their diagnosis and treatment for breast cancer. Table 2 summarizes the responses from BCS when asked how their music listening behavior had changed since breast cancer treatment. While some women reported a small change in music listening and enjoyment, the vast majority of women reported that their feelings about music and their listening habits had not changed since cancer treatment.

Overall, results of the music cognition tests revealed a mean (SD) global score of 79% (10%) correct responses for BCS and 80% (9%) for HC. These scores are significantly below (P value = .002 and .003, respectively) the standard global composite score on the MBEA, mean (SD) of 86% (6%), normed on 50 women aged 40 to 79 years. To investigate our main question, we calculated the differences in music cognition variables between BCS and HC, controlling for PTA. Table 3 contains means and SDs on all of the music cognition variables with corresponding confidence intervals and effect sizes. The effect sizes in the contour, interval, and tonality perception tasks suggest that there may be differences between the 2 groups in melodic

Table 2. Frequencies of BCS's Feelings About Music Since Treatment (N = 28)

	Not at All	A Little	Moderately	Quite a Bit	Extremely	Missing
My enjoyment of music has changed	22	3	1	1	1	
The way I listen to music has changed	20	4	3	1		
Music sounds different	25	2				1
I am more emotional when listening to music	19	9				
I enjoy music more	19	7	1	1		
My music tastes/preferences have changed	20	6	1	1		

Abbreviation: BCS, breast cancer survivors.

Table 3. Means and SD for Music Cognition Variables[a]

Variable	Group	N	Mean	SD	Estimated[b] Mean Difference (Standard Error)	95% CI[b] Lower Bound	Upper Bound	Effect Size[b,c]	*P* Value[b] (2-Tailed)
Contour	BCS	56	24.11	3.56	−1.15 (0.92)	−3.03	0.73	0.24	.22
	HC		24.96	2.87					
Intervals	BCS	56	22.14	4.53	−1.21 (1.13)	−3.54	1.13	0.20	.30
	HC		22.89	4.60					
Tonality	BCS	56	25.39	3.27	−1.27 (0.82)	−2.96	0.41	0.29	.13
	HC		26.36	3.36					
Rhythm	BCS	56	25.04	3.92	−0.21 (0.96)	−2.19	1.77	0.04	.83
	HC		25.15	2.80					
Meter	BCS	54[d]	23.52	5.34	−0.14 (1.28)	−2.77	2.50	0.02	.92
	HC		23.44	4.87					
Melodic Memory	BCS	54[d]	24.93	4.13	0.72 (1.09)	−1.52	2.96	0.13	.51
	HC		23.85	4.23					
MBEA Average	BCS	54[d]	24.19	3.10	−0.55 (0.77)	−2.15	1.04	0.14	.48
	HC		24.46	2.91					

Abbreviations: BCS, breast cancer survivors; CI, confidence interval; HC, healthy controls; MBEA, Montreal Battery Evaluation of Amusia; PTA, pure tone average; SD, standard deviation.
[a]Higher score = better performance on all MBEA variables.
[b]Estimated from a linear mixed model adjusting for PTA.
[c]Absolute value of the estimated mean difference/SD of the difference.
[d]One BCS participant did not complete the music cognition testing, the pair was removed for 3 variables.

organization, with HC scoring slightly but not significantly better than BCS.

Discussion

The BCS report changes in cognitive functioning after adjuvant chemotherapy treatment, which have been demonstrated with objective cognitive testing across several studies.[6,7] The most common complaints are in the domains of verbal memory, executive functioning, and psychomotor speed. Mechanisms of melodic organization such as pitch recognition and processing have been linked to neural circuits related to working memory, attention, language processing, and spatial processing in healthy populations and in lesion studies.[33-36] While music cognition is a form of general cognition, to our knowledge changes in music cognition related to receiving chemotherapy treatment for breast cancer have not previously been explored.

The purpose of this pilot study was to compare hearing thresholds and music cognition skills between BCS and age-matched HC. There was no evidence of differences in hearing threshold related to receiving chemotherapy treatment. However, hearing thresholds were significantly negatively correlated with performance on the 3 melodic organization subtests. There was no correlation, however, between hearing threshold and performance on the temporal organization subtests. This pattern of results is similar to findings from several studies of hearing-impaired children and adults who use cochlear implants.[30,37-39] That is, hearing-impaired listeners have significant deficits in melodic perception but intact temporal perception. The entire sample of women in the present study also performed significantly below the standard global composite score on the MBEA. It is possible that the women in our sample had worse hearing thresholds than the participants with whom the MBEA was normed.

The differences in music cognition variables between BCS and HC were not statistically significant, but effect sizes suggest that with increased power there may be significant differences between the 2 groups. A closer examination of individual music cognition variables may help define future areas of inquiry. Greatest differences between groups were noted on the tasks that assessed pitch or melodic organization rather than temporal organization. Again, the pattern of results is quite similar to that of hearing-impaired listeners in similar music perception tests.[30,37,39,40] Moreover, many researchers have found that adults with amusia experience melodic organization deficits but have intact temporal organization skills.[41] It is possible that both hearing loss and cancer treatment using potentially ototoxic drugs result in some degree of acquired amusia.

Contrary to expectations, BCS scored better on melodic memory than HC. This finding could be due to enhanced strategies that BCS use to overcome encoding issues for memory. That is, the BCS participants have had months to years to adapt to their general cognitive changes, and it is possible that they use special mnemonic or other strategies to increase their encoding skills, working memory, and recognition memory. Correlating our findings with standardized cognitive tests would assist in understanding these particular results.

Overall, the present findings suggest that differences in music perception skills across BCS and HC participants may be slight. Based upon the effect sizes observed in this pilot study for contour, intervals, and tonality, studies with a similar design would need 200 pairs of BCS and HC to have 80% power to detect an effect using a paired *t* test at a level of significance of .05. Along with a fully powered follow-up study, additional studies exploring the relationship between music cognition and general cognitive functioning in cancer survivors may point to clinical meaningfulness of the music perception findings and interventions to help BCS adapt to or overcome persistent cognitive difficulties.

Declaration of Conflicting Interests

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