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Relating quality of life to outcomes and predictors in adult cochlear implant users: Are we measuring the right things?

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Abstract

Objective: Current clinical outcome measures for adults receiving cochlear implants (CIs) consist of word and sentence recognition, primarily under quiet conditions. However, these measures may not adequately reflect patients' CI-specific quality of life (QOL). This study first examined traditional auditory-only speech recognition measures and other potentially relevant auditory measures as correlates of QOL in CI users. Second, scores on non-auditory tasks of language and cognition were examined as potential predictors of QOL.

Study Design: Twenty-five postlingually deafened adults with CIs were assessed.

Methods: Participants completed a validated CI-specific QOL measure (the Nijmegen Cochlear Implant Questionnaire, NCIQ) and were tested for word and sentence recognition in quiet, as well as sentence recognition in speech-shaped noise. Participants also completed assessments of audiovisual speech recognition, environmental sound identification, and a task of complex auditory verbal processing. Several non-auditory language and cognitive tasks were examined as potential predictors of QOL.

Results: QOL scores significantly correlated with scores for audiovisual speech recognition and recognition of complex sentences in quiet, but not sentences in noise or isolated words. No significant correlations were obtained between QOL and environmental sound identification or complex auditory verbal processing. QOL subdomain scores were predicted by several non-auditory language and cognitive tasks as well as some patient characteristics.

Conclusion: Postoperative measures of recognition of sentences in quiet and audiovisual sentence recognition correlate with CI-related QOL. Findings suggest that sentence recognition

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tasks are QOL-relevant outcomes, but explain only a small fraction of the variability in QOL outcomes for this patient population.

Keywords

Cochlear implants; Cognition; Speech perception; Quality of life

Introduction

Cochlear implants (CIs) have dramatically improved the lives of adults with postlingual deafness.¹ In recent years, interest has grown in assessing health-related quality of life (QOL), specifically the impact of CIs, both as a way to demonstrate the cost-effectiveness of cochlear implantation, and to examine the functional impact of CIs more broadly.²⁻⁶ However, QOL measures are not routinely obtained clinically; instead, postoperative assessments generally consist of CI-aided speech recognition, most often in quiet. Because the principal motivation of most CI candidates is to improve speech recognition, it may be hypothesized that this outcome will be directly related to post-implant QOL. However, other non-auditory measures have also been shown to affect QOL scores in CI patients.⁶ This study was conducted, first, to determine the relationship between speech perception and patient-centered QOL outcomes in adult CI users, and, second, to investigate which non-auditory abilities and patient characteristics may predict CI-related QOL outcomes.

Several studies have examined relations between measures of speech recognition and QOL, and results are inconsistent. A few studies have identified small-to-medium correlations between post-implantation speech recognition scores and QOL.⁷⁻¹¹ Other studies have failed to identify significant correlations.¹²⁻¹³ Thus, it is still not clear if clinical measures of speech recognition are appropriate indicators of patient-centered QOL outcomes. If not, then perhaps CI-related QOL should serve as a more foundational outcome measure when examining cost-effectiveness of cochlear implantation, as well as when pursuing expanded insurance coverage for patients who could benefit from implantation.

If clinical speech perception performance does not reliably reflect QOL following cochlear implantation, what key outcome variables are we overlooking? One consideration may be to include assessments that broaden evaluation of communication and functional abilities. For example, it is likely that patients' abilities to understand speech under noisy conditions would better reflect their communication abilities than speech recognition in quiet. Likewise, patients' abilities to understand speech that is delivered audiovisually (i.e., auditory input with lip-reading) are likely more relevant to their reported QOL using their devices. For example, CI patients most commonly find themselves in communicative situations with combined audiovisual input.¹⁴ Additionally, the ability to identify environmental sounds, which self-reports demonstrate to be a goal of implant candidates second only to speech perception, may relate to individuals' reported QOL.¹⁵⁻¹⁷ Finally, the capacity to perform more challenging cognitive tasks using speech input may represent how adept a patient is at using auditory input during more cognitively demanding communicative tasks. To address these concerns, the first goal of the current study was to examine how self-reported QOL of adult CI users related to more traditional auditory measures of word and sentence

recognition in quiet, but also to less commonly used measures of speech recognition in noise, audiovisual speech perception, environmental sound identification, and cognitive processing of auditory verbal information.

The second aim of the current study was to examine more sensitive measures of language skills and cognitive functions for their ability to predict QOL outcomes, using non-auditory measures to eliminate the confounding effects of audibility. In particular, measures were selected to assess linguistic and cognitive abilities that could reasonably be expected to play a role in the communicative functioning of patients with hearing loss: working memory (the ability to store and manipulate verbal information), rapid verbal processing, inhibition-concentration function (the ability to provide sustained attention for a task and to inhibit responses to extraneous sensory input), lip-reading ability, visual linguistic closure (the ability to use surrounding context to recognize degraded sentences), and general intelligence and reasoning abilities. Identifying non-auditory measures that can predict postoperative QOL outcomes in CI users could provide a basis for development of clinical measures to improve preoperative counseling. Previous studies have found that worse preoperative hearing and longer duration of deafness are associated with better postoperative QOL, likely as a result of having more to gain from implantation or different outcome expectations.^{7,18} However, beyond traditional patient/audiologic factors, few QOL predictors have been identified. It is conceivable that better preoperative language knowledge and cognitive functioning would predict better QOL outcomes, because these skills assist CI users in optimizing their abilities to function in daily life with their implants.

To accomplish the two aims of this study, a group of adult CI users with at least two years of CI experience were assessed for CI-specific QOL using a validated self-report questionnaire, the Nijmegen Cochlear Implant Questionnaire (NCIQ).²⁰ Participants were also administered several measures of speech recognition for words and sentences in quiet and sentences in noise, along with recognition of speech presented audiovisually, identification of common environmental sounds, and the ability to perform a cognitively challenging task using auditory verbal stimuli (a listening span task of complex working memory - LSPAN). Finally, patients underwent testing using non-auditory measures of working memory, rapid verbal processing, inhibition-concentration, lip-reading ability, visual linguistic closure, and general intelligence and reasoning skills.

Methods

Participants

Twenty-five adult CI users from The Ohio State University were enrolled, all with at least two years of CI experience (average 7.5), and ranging between the ages of 50 and 83 (average 69.1) years. See Appendix A for details regarding participants. Data regarding demographics and audiologic factors are shown for the 25 CI participants in Table 1.

Procedures

All testing was completed at the Eye and Ear Institute (EEI) of The Ohio State University Wexner Medical Center after Institutional Review Board (IRB) approval, and informed

written consent was obtained from all patients. All participants were tested wearing their usual auditory prostheses (unilateral CI, bilateral CIs, or CI with a contralateral hearing aid, as appropriate), which were confirmed to be functioning appropriately at the start of testing. No patients used combined electric-acoustic stimulation in the implanted ear. Some scores from testing were reported previously.^{19–20}

QOL Measure

Nijmegen Cochlear Implant Questionnaire (NCIQ): Details of this measure can be found in Appendix B. Measures were completed by participants at home with no time limit. The NCIQ encompasses hearing and speech, psychological, and social domains.²¹ Individual subdomain scores, as well as total scores across subdomains, were used in analyses, with higher scores representing better QOL.

Speech Recognition—Speech recognition was tested using several types of speech materials: CID-22 words²² in quiet; long, complex, and semantically meaningful IEEE sentences²³ in quiet; PRESTO sentences²⁴ in quiet; and short, meaningful sentences as well as long, complex sentences in speech-shaped noise at +3 dB SNR. Each word or sentence was presented, and the participant was asked to repeat what was heard. All materials were presented at 68 dB SPL over a loudspeaker positioned one meter from the participant at 0° azimuth. Dependent measures were percent correct words. Details of speech recognition measures are provided in Appendix C.

Other Auditory Outcome Measures—Additional auditory outcome measures were collected to examine as correlates with QOL. These included audiovisual sentence recognition in quiet using CUNY sentences,²⁵ a task of environmental sound identification using the Familiar Environmental Sound Test-Identification (FEST-I),^{16,26} and a task of complex auditory verbal processing using the Listening Span (LSPAN) task. Details of these auditory measures are also provided in Appendix C.

Non-auditory Cognitive and Language Measures—Six non-auditory measures were collected to examine as predictors of QOL. The tests were selected based on previous research that has suggested the involvement of the underlying abilities in speech perception and language processing.^{27–31} Verbal working memory was assessed using a visual Digit Span task. Rapid verbal fluency and phonemic decoding of written materials was evaluated using the Test of Word Reading Efficiency (TOWRE).³² Inhibition-concentration was assessed using a computerized Stroop task.³³ Lip-reading ability was assessed using a list from the CUNY corpus.²⁵ A visual Fragmented Sentences test was used to assess linguistic closure ability. The Ravens Matrices task of general intelligence was used to assess nonverbal reasoning.³⁴ Details of these tasks can be found in Appendix D.

Data Analyses

To address the first aim, Pearson product moment correlation analyses were performed among QOL and auditory-related outcome measures. To address the second aim, Pearson correlations were performed, followed by unit weighting analysis,³⁵ to identify non-auditory

language and cognitive factors that can best predict QOL scores. Details regarding unit weighting analysis and rationale for this approach can be found in Appendix E.

Results

The first question of interest was whether QOL scores would correlate with auditory-related outcome scores. There was a broad range of QOL outcomes, shown in Table 2. Table 3 shows results of the correlation analyses with the auditory measures. Total QOL sum scores correlated moderately only with scores of sentence recognition in quiet for IEEE sentences. IEEE sentence scores were also moderately correlated with NCIQ subdomains of Advanced Sound Perception, Speech Production, and Social Interactions. Scores on the Speech Production subdomain also correlated with two other tests: word recognition in quiet and sentence recognition in quiet assessed with PRESTO. Scores on PRESTO sentences also correlated with those on the Social Interaction subdomain of NCIQ, while scores on audio-visual sentence recognition in quiet correlated with both Social Interaction and Self-esteem subdomains. However, application of a Holm-Bonferroni correction revealed that only correlations of the Social Interaction subdomain with PRESTO sentences and audio-visual sentence recognition scores remained significant at $p < 0.05$. Otherwise, QOL scores did not correlate with isolated word recognition, environmental sound identification, or complex auditory verbal processing, nor did they generally correlate with scores of recognition of sentences in noise.

The second question of interest was whether any non-auditory language or cognitive test scores would correlate with QOL scores. Pearson bivariate correlations between individual non-auditory tests and NCIQ scores are shown in Table 4. Total QOL sum scores did not correlate with any single measure. Moderate correlations were found among several cognitive tasks and subdomains of the NCIQ. Following a Holm-Bonferroni correction, however, only correlations of Advanced Sound Perception with Ravens Reasoning test and Speech Production with TOWRE Rapid Reading test scores remained significant at $p < 0.05$. A unit weighting analysis revealed that combined normalized scores of two predictor variables, the TOWRE Rapid Reading test and Ravens Reasoning test, correlated significantly with the Advanced Sound Perception ($r = .51, p < .01$), Speech Production ($r = .54, p < .01$), as well as total NCIQ scores ($r = .40, p < .05$). Adding other non-auditory linguistic or cognitive predictor scores did not lead to greater correlation magnitudes for any subdomain of NCIQ.

As an exploratory measure, NCIQ scores were further correlated with patients' characteristics that have previously been identified as possible predictors of CI-specific QOL:⁶ patient age at the time of study, duration of deafness prior to CI, age at hearing loss onset, and the number of years of CI use. Pearson bivariate correlations between patient characteristics and NCIQ scores are shown in Table 5. Total QOL sum scores did not correlate with any single measure. Moderate bivariate correlations were identified for some patient characteristics and QOL subdomain scores. However, a Holm-Bonferroni correction indicated that only the correlation between patient age and the Advanced Sound Perception subdomain remained significant at $p < 0.05$. Next, to assess the combined predictive power of three orthogonal patient characteristics, age at the time of study, age at hearing loss onset,

and duration of CI use were combined in a unit weighting analysis. This analysis revealed that these three variables were moderately and significantly correlated with several subdomain QOL scores as well as Total NCIQ scores. These correlations further indicate that patient characteristics may play a significant role in predicting patients' QOL with their CIs.

Discussion

The purpose of the reported study was two-fold: (1) to investigate which auditory outcome measures are most strongly related to patient QOL after cochlear implantation; and (2) to identify non-auditory linguistic and cognitive factors that could serve as predictors of CI-related QOL. Regarding the first goal, findings suggest that speech recognition tests, primarily sentence recognition in quiet along with recognition of audio-visual sentences, correlate the most with CI-related QOL after implantation. The same was not true for recognition of isolated words in quiet. These findings replicate those of our previous report.⁷ Here we demonstrate significant NCIQ correlations with IEEEE and PRESTO sentence scores in quiet. Notably, the IEEEE sentences are challenging sentences, and the PRESTO sentences introduce high variability in talker and dialect, both of which may be more relevant to everyday functioning for CI users. The weak-to-moderate magnitude of QOL correlations with various speech metrics seems to be consistent with previous studies using the NCIQ.^{10,21,36} Moreover, those correlations generally became non-significant when corrected for multiple comparisons. Nonetheless, these findings do suggest that sentence recognition in quiet may reflect, to a relatively limited degree, QOL for CI users.

Considering our other potentially more ecologically valid auditory outcome measures, a correlation of QOL with audio-visual sentence recognition was identified for the Social Interactions subdomain of the NCIQ, and this remained significant after Holm-Bonferroni correction. This finding is consistent with self-reports that for adults with CIs, the most common communication setting encountered in daily life is speech from another person with the speaker's face visible.¹⁴

In contrast, we did not find any significant correlations of QOL with the other auditory tests that were considered more representative of everyday functioning such as environmental sound identification. However, it is possible that this skill alone may not play a strong role in QOL, or the environmental sounds used in this study were not highly relevant to daily life. The LSPAN task is a challenging and artificial auditory task; it is possible that this task was too challenging to accurately reflect the cognitive processing load experienced by CI users during daily auditory processing. Perhaps more likely, the lack of strong association with speech tests may indicate that speech perception ability plays a lesser role in QOL scores in highly experienced CI users. In fact, most of the participants in our study were long-time CI users with the average of 7.5 years of CI experience, and their speech recognition abilities had likely stabilized over multiple years of CI use. Having come to expect a certain level of speech performance, their responses to NCIQ questions may have been less affected by their speech perception scores. This interpretation is consistent with previous research which indicates a slight decline in NCIQ metrics following long-time implant use.³⁶ The influence

of speech perception abilities on NCIQ scores may be quite different in newly implanted individuals whose speech perception abilities undergo rapid positive changes.

Regarding our second goal, to identify non-auditory linguistic and cognitive predictors of CI-related QOL, this study identified two useful predictors of QOL, at least among some subdomains of the NCIQ: rapid reading and general intelligence and reasoning. A combination of these two tests, as indicated by the results of the unit weighting analysis, may further expand their ability to predict aspects of QOL in CI patients.

Third, our exploratory analysis further indicates that patients' characteristics play an important role in predicting their CI-related QOL. Just like non-auditory cognitive abilities, patient characteristics are not directly related to patients' speech perception and performance on other auditory tasks. Thus, these findings suggest the potential utility of these non-auditory variables in investigating their capacity as preoperative clinical prognosticators of CI-related QOL.

This study has several limitations. First, we only examined postoperative QOL in highly experienced CI users. As mentioned above, it is possible that the influence of specific auditory tests on QOL may differ before implantation and at different time points following implantation, or be influenced by individual expectations or pre-implantation goals of our patients. Second, the sample size was small; however, a large amount of data was collected for each patient included in the study, which allowed more in-depth analyses of correlations and predictors of QOL. Third, our study sample consisted of a group of primarily older adults, most of whom had presbycusis or progressive hearing loss during adulthood, who were implanted for severe-to-profound hearing loss. Thus, findings may not generalize to other groups of CI users (e.g., younger patients with other etiologies of hearing loss, patients with more residual hearing or who use combined electric-acoustic stimulation in one ear, patients with CIs for single-sided deafness). Our study sample was otherwise fairly heterogeneous, including some patients using unilateral CIs, some with bilateral CIs, and some using bimodal stimulation, making it impossible to attribute findings to device status. Lastly, our QOL measure, the NCIQ, may itself have several limitations. The NCIQ was designed as a disease-specific health related QOL measure that has been previously utilized by this group of investigators and others,^{7,12} motivating its selection here to facilitate comparisons. An alternative QOL measure that has been used with some frequency in evaluating the impact of audiological interventions (including CIs) is the Glasgow Benefit Inventory (GBI).³⁷⁻⁴⁰ The GBI is not disease-specific like the NCIQ, but was designed for the purpose of assessing patient QOL following otorhinolaryngological surgery. Another consideration is whether QOL questionnaires that are tailored towards assessing the effects of aging should be incorporated for this patient population. Ultimately, by broadening our assessment tools for QOL, additional contributors may become evident.

Conclusion

For adult CI users, scores of recognition of challenging sentences in quiet and audio-visual sentence recognition moderately correlated with CI-related QOL. Several non-auditory linguistic and cognitive measures, as well as patient characteristics, served as predictors of at

least some subdomains of CI-related QOL. Results provide a basis for further validation of currently identified predictors with a larger CI patient sample. These findings suggest a persistent need to develop useful clinical measures to prognosticate outcomes for adult patients who undergo cochlear implantation, which would assist clinicians in counseling patients on the likely benefits they will receive from implantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Cochlear implant (CI) user demographics. PTA: Better ear unaided four-tone pure tone average at .5, 1, 2, and 4 kHz; B: Bilateral; R: Right; L: Left

Table 1.

Participant	Gender	Age (years)	Implantation Age (years)	Duration of CI Use (years)	Side of Implant	Hearing Aid	Etiology of Hearing Loss	Better Ear PTA (dB HL)
1	F	65	54	11	B	N	Genetic, progressive as adult	120
2	F	66	62	4	R	Y	Genetic, progressive as adult	78.8
3	F	67	58	9	R	Y	Genetic, progressive as adult	103.8
4	M	70	65	5	R	N	Genetic, progressive as adult	88.8
5	F	57	48	9	R	Y	Genetic, progressive, noise	82.5
6	M	79	76	3	R	Y	Genetic, progressive	70
7	F	69	56	13	B	N	Otosclerosis	112.5
8	M	55	50	5	B	N	Progressive as adult	120
9	F	76	68	8	L	N	Progressive, autoimmune	108.8
10	M	79	74	5	L	N	Progressive as adult	108.8
11	F	81	71	10	R	N	Progressive, sudden hearing loss	88.8
12	M	59	57	2	B	N	Sudden hearing loss	120
13	M	78	72	6	B	N	Progressive as adult	120
14	M	69	62	7	B	N	Genetic, progressive	120
15	F	50	35	15	B	N	Progressive as child and adult	117.5
16	F	64	61	3	R	N	Progressive as adult	103.8
17	F	67	58	9	B	N	Meniere's	120
18	M	83	76	7	R	Y	Progressive as adult, noise	68.8
19	F	73	67	6	R	N	Progressive as child and adult	98.8
20	M	76	73	3	L	Y	Progressive, infections	72.5
21	F	79	45	34	R	Y	Progressive as adult	57.5
22	M	74	72	2	R	Y	Progressive as child and adult	92.5
23	M	66	60	6	L	N	Meniere's	80
24	F	65	63	2	R	N	Genetic, progressive as adult	86.3
25	F	62	59	3	B	N	Sepsis, ototoxicity	95
Mean / %	56% F	69.1	61.7	7.5	48% R	32% Y		97.2
St. Dev.		8.6	10.3	6.5	16% L			19.7
					36% B			

Table 2.

Means and ranges of performance on tasks of quality of life, speech recognition, other auditory outcome measures, and non-auditory language/cognitive predictor measures. NCIQ: Nijmegen Cochlear Implant Questionnaire. LSPAN: Listening Span task of auditory verbal working memory capacity

	Mean	N	(Min-Max)
Quality of Life			
NCIQ (sum score)	417.1	25	(264-554)
Physical - Basic sound perception	64.5	25	(30-100)
Physical - Advanced sound perception	81.5	25	(50-100)
Physical - Speech production	61.4	25	(28-98)
Psychological - Self-esteem	70.7	25	(22-92)
Social - Activity limitations	74.7	25	(28-98)
Social - Social interactions	64.3	25	(24-85)
Speech Recognition (percent words correct)			
Words in quiet	74.3	23	(26-98)
IEEE Sentences in quiet	77.4	24	(45.3-90.7)
PRESTO Sentences in quiet	65.6	24	(12.1-96.9)
High-context Sentences in noise	46.8	21	(0-97.6)
Complex Sentences in noise	28.4	21	(1-76.8)
Other Auditory Outcome Measures			
Audiovisual sentence recognition (percent words correct)	92.3	25	(52-100)
Environmental sound identification (percent correct)	63.8	25	(40-88)
LSPAN (total correct letters)	27.4	17	(0-57)
Non-auditory Predictor Measures			
Digit span (total digits correct)	42.9	25	(14-79)
Rapid reading (percent words correct)	73.3	25	(55-89)
Inhibition-concentration (response time congruent, milliseconds)	1434.5	25	(828-2824)
Inhibition-concentration (response time incongruent, milliseconds)	1859.6	25	(845-6397)
Lip reading sentences (percent words correct)	10.0	25	(0-54)

Table 3.

Correlations of NCIQ quality of life scores and auditory measures.

<i>r</i> values	Word recognition in quiet	IEEE sentence recognition in quiet	PRESTO sentence recognition in quiet	Short sentence recognition in noise	Long, complex sentence recognition in noise	Audiovisual sentence recognition in quiet	Environmental sound identification (percent correct)	Complex auditory verbal processing (LSPAN - total correct letters)
NCIQ (sum score)	0.19	0.4*	0.38	0.18	0.24	0.36	0.24	0.01
Physical - Basic sound perception	-0.05	0.01	0.01	0.01	0.02	-0.02	-0.09	-0.16
Physical - Advanced sound perception	0.17	0.43*	0.25	0.11	0.22	0.09	0.34	0.42
Physical - Speech production	0.41*	0.49*	0.41*	0.31	0.37	0.31	0.32	0.28
Psychological - Self-esteem	0.19	0.31	0.33	-0.01	0.06	0.43*	0.21	-0.31
Social - Activity limitations	-0.01	0.26	0.35	0.1	0.14	0.34	0.16	-0.26
Social - Social interactions	0.28	0.48*	0.53**	0.38	0.37	0.62**	0.27	-0.11

* Values with have *p* value <.05

** Values with have *p* value <.01

Table 4. Correlations of non-auditory language and cognitive scores with quality of life. NCIQ: Nijmegen Cochlear Implant Questionnaire

<i>r</i> values	Digit Span (total correct)	Rapid Reading (percent correct)	Inhibition-Concentration (response time congruent)	Inhibition-Concentration (response time incongruent)	Lip Reading (percent words correct)	Visual Fragmented Sentences (percent sentences correct)	Ravens Reasoning (number correct)	Rapid Reading and Ravens Reasoning
NCIQ (sum score)	0.06	0.37	-0.24	-0.18	0.31	0.25	0.33	0.40 *
Physical - Basic sound perception	0.22	0.13	0.07	-0.02	0.17	0.05	0.08	0.12
Physical - Advanced sound perception	0.07	0.37	-0.13	-0.02	0.29	0.40 *	0.53 **	0.51 **
Physical - Speech production	0.00	0.53 **	-0.20	-0.25	0.30	0.28	0.43 *	0.54 **
Psychological - Self-esteem	0.01	0.27	-0.21	-0.21	0.29	0.15	0.16	0.24
Social - Activity limitations	-0.05	0.15	-0.23	-0.01	0.22	0.18	0.15	0.17
Social - Social interactions	0.05	0.37	-0.50 **	-0.37	0.27	0.19	0.3	0.36

* Values with have *p* value <.05

** Values with have *p* value <.01

Table 5. Selected patient characteristics as predictors of quality of life. NCIQ: Nijmegen Cochlear Implant Questionnaire

<i>r</i> values	Age at study (years)	Duration of deafness before implantation (years)	Age at hearing loss onset (years)	Duration of CI use (years)	Age at study, age at hearing loss onset, and duration of CI use (years)
NCIQ (sum score)	-0.28	0.22	-0.38	0.08	-0.55 *
Physical - Basic sound perception	-0.16	0.27	-0.36	0.09	-0.47
Physical - Advanced sound perception	-0.57 **	0.10	-0.41 *	0.30	-0.25
Physical - Speech production	-0.45 *	0.01	-0.21	-0.13	-0.62 *
Psychological - Self-esteem	-0.07	0.18	-0.21	-0.23	-0.58 *
Social - Activity limitations	0.04	0.23	-0.32	0.51	-0.07
Social - Social interactions	-0.12	0.29	-0.34	-0.26	-0.62 *

* Values with have *p* value <.05

** Values with have *p* value <.01