Original Article

Cross-Modal Cortical Activity in the Brain Can Predict Cochlear Implantation Outcome in Adults: A Machine Learning Study

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OBJECTIVES: Prediction of cochlear implantation (CI) outcome is often difficult because outcomes vary among patients. Though the brain plasticity across modalities during deafness is associated with individual CI outcomes, longitudinal observations in multiple patients are scarce. Therefore, we sought a prediction system based on cross-modal plasticity in a longitudinal study with multiple patients.

METHODS: Classification of CI outcomes between excellent or poor was tested based on the features of brain cross-modal plasticity, measured using event-related responses and their corresponding electromagnetic sources. A machine learning estimation model was applied to 13 datasets from 3 patients based on linear supervised training. Classification efficiency was evaluated comparing prediction accuracy, sensitivity/specificity, total mis-classification cost, and training time among feature set conditions.

RESULTS: Combined feature sets with the sensor and source levels dramatically improved classification accuracy between excellent and poor outcomes. Specifically, the tactile feature set best explained CI outcome (accuracy, 98.83 ± 2.57%; sensitivity, 98.00 ± 0.01%; specificity, 98.15 ± 4.26%; total misclassification cost, 0.17 ± 0.38; training time, 0.51 ± 0.09 sec), followed by the visual feature (accuracy, 93.50 ± 4.89%; sensitivity, 89.17 ± 8.16%; specificity, 98.00 ± 0.01%; total misclassification cost, 0.65 ± 0.49; training time, 0.38 ± 0.50 sec).

CONCLUSION: Individual tactile and visual processing in the brain best classified the current status when classified by combined sensor–source level features. Our results suggest that cross-modal brain plasticity due to deafness may provide a basis for classifying the status. We expect this novel method to contribute to the evaluation and prediction of CI outcomes.

KEYWORDS: CI outcome, cross-modal plasticity, predicting factor, electroencephalography, machine-learning, tactile

INTRODUCTION

Prediction of the benefit by cochlear implantation (CI) is often difficult because outcomes vary among patients. Multiple factors have been tested to identify those that best predict speech perception after CI, such as the duration of deafness, age at implantation, and length of CI usage.[1,2]

However, the duration of deafness only explains 20% of outcomes, as evidenced by a histopathological study.[3] Moreover, Gantz et al. tested several predictive candidate factors in 48 post-lingual deaf adults; they observed no relationship with the duration of deafness but found positive correlations ($r = 0.81$) with the Iowa Sentence Test and the Northwestern University Auditory Test No. 6 word score,[4] which were weak relationships.

Kang et al.[5] acknowledged the importance of predictive factors after CI and discussed the limiting factors between good and poor outcome groups. Prenatal problems ($P = .005$; odds ratio (OR), 4.878) and a narrow bony cochlear nerve canal ($P = .046$; OR,

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4.785) differed significantly between groups, as well as inner ear (P = .003) and intraoperative (P = .045) problems. The timing of implantation did not contribute to prediction of outcomes in their cohort, presumably due to the participants being pre-lingual.

Electrophysiological observations are used to identify interrelationships with speech performance after CI. The pre-operative auditory brainstem response and area ratio of the vestibulocochlear nerve have been proposed as optimal predictors of CI outcomes in patients with a cochlear nerve deficiency,[6] but these factors did not predict sufficiently.

Cortical plasticity has recently been discussed in the context of auditory deprivation and the potential for reversal after CI. A positive correlation was detected between high speech performance and regional cerebral blood flow (rCBF) level in the auditory brain regions using ^{18}F-fluorodeoxyglucose ([^{18}F]-FDG) positron emission tomography imaging.[7] Moreover, a possibility of the functional relationship between visual activity and CI outcome was addressed as functionally relevant. Giraud and Truy focused on the visual dependency of patients who had undergone CI in terms of speech comprehension; they found robust activation in the visual face area in CI users.[8] Kang et al. also observed a significant increase in [^{18}F]-FDG uptake in the medial visual areas, but this was not correlated with patient outcomes.[9] Additionally, Green et al. reported no significant increase of visual activity at 1 year after CI; no significant changes of lateralization in auditory cortical activation were observed either at the time of CI or during the first-year imaging results.[10]

Kim et al.[11] reported the auditory–visual cross-modal plasticity as a predictive factor of CI outcomes. In the poorly performing CI group, P1 evoked by visual stimuli showed enhanced amplitude in the temporal region, comparable to the good performance CI group. The poor performance CI group also showed reduced amplitude of P1 in the occipital region, unlike the good performance and control groups. They concluded that insufficient restoration of the auditory circuit might have caused negative performance after CI. Even though the test was performed only after CI, this result shed implicative light on the possibility of a cross-modal plasticity as a predicting factor.

For the longer follow-up study up until 27 months after CI, Glick and Sharma concluded that a significant benefit had been conferred in a child with single-sided deafness; moreover, they found clear reversal

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MAIN POINTS

- Variability in outcomes after cochlear implant impedes the estimation of its benefit.
- Using electroencephalography (EEG), we sought objective factors of cortical plasticity that best predict CI outcomes.
- Datasets were trained and validated using a support vector machine (SVM) classification.
- Tactile and visual responses in the brain contribute the most to predicting outcomes.
- The combined features of sensor and source levels revealed a clear advantage of classification.

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of somatosensory recruitment and only residual visual cross-modal plasticity.[12] Despite the single case result, the study may provide the possibility of the cross-modal plasticity as a predicting factor.

The aforementioned studies indicate the difficulty of extracting predictive factors for CI outcomes, as there is wide variability among patients. Machine learning can be of use for extracting elements from multiple factors, based on supervised or non-supervised learning (machine learning). Attempts have been made using machine learning to extract factors that best explain various diseases or various states (or severity) of a disease such as predicting survival period in colon cancer[13] or identification of schizophrenia from the normal.[14] Most common machine learning estimation models apply linear supervised training. In electrophysiological research, P300[15] or mismatch negativity[16] components render shared features, because these components are known to represent cortical indicators associated with cognitive decline.

Because electroencephalography (EEG) provides non-invasive and objective measurements, we sought to develop EEG biomarkers to evaluate and predict CI outcomes. Our hypothesis is based on the cortical cross-modal neuroplasticity as an affecting factor. Using 3 different feature sets (sensor-level, source-level, and combined-level), good and poor outcomes were classified in multiple patients and at multiple time points after CI.

METHODS

Datasets

All the data acquisition was approved by the institutional review board of our hospital and was conducted in compliance with the Declaration of Helsinki, International Conference on Harmonization Guidelines for Good Clinical Practice. Data were acquired at a maximum of 5 time points for each patient; before CI, and at 3, 6, 12, and 18 months after CI. At each time point, speech recognition score (SRS) was generated using a mono-syllable word test. Group definitions were based on a cutoff threshold of 70%: group 1 was assigned when SRS was >70 and group 2 was assigned when SRS was ≤70%, based on the institutional criteria.

EEG Recording and Pre-processing

Scalp EEG data were recorded using CURRY 7 software and a SynAmps2 amplifier (Compumedics, Neuroscan, Charlotte, NC, USA) from 64 Ag/AgCl scalp electrodes, which were evenly arranged based on the 10-20 electrode system. The ground was placed on the forehead, while the references were linked to the ears (after CI, the reference was placed contralateral to the CI side). In addition, eye movements were recorded using a vertical and horizontal electrooculogram, along with an electrocardiogram. Impedances were kept below 5 kΩ throughout the recording. Two or three electrodes at the CI site were excluded. Signals were 0.1-200 Hz band-pass filtered (60 Hz power-line notched) on-line at a sampling rate of 1000 Hz.

Stimuli and Tasks

Cortical auditory evoked potentials (cAEPs) were evoked using a 90-ms /ba/ sound recorded by a female speaker.[12] Cortical somatosensory evoked potentials (cSEPs) were generated by a series of 20 ms tactile stimulation on the median nerve of the hand, using a stimulator (D268, UK). The inter-stimulus intervals were randomized

but 2 stimulations were at least 700 ms apart; the intensity was fixed at a sub-threshold of 70-80% of the individual motor threshold. Participants were instructed to enjoy a silent movie on a PC monitor. Pattern reversal consisting of a pair of checkerboards was used for the cortical visual evoked potentials (cVEPs) because there was more inter-subject VEP variability, relative to flash or pattern onset stimuli.

Sensor-Level Feature Set

The standard pipeline was included, such as eye-blinking artifacts and CI-associated and other gross artifacts, which were removed based on independent component analysis and second-order blind inference[17] and further visual inspection. Cleaned data were band-pass filtered at 1-50 Hz. Across modalities, epochs were rejected when the amplitude exceeded $\pm$ 100 μV or the slope was not natural to human physiology. Peaks and latencies were computed across all electrodes. CI-side electrodes were interpolated using spherical spline interpolation, in accordance with the method of Perrin et al.; this method produces better results, although it depends on an infinite series in which the sum is not easily expressed, in contrast to pseudo-spherical spline surfaces.[18]

The data of event-related potential (ERP) were epoched 500 ms post-stimulus onset, including a baseline of 100 ms. The remaining artifact-free trials were 75-90% (cAEP), 80-95% (cSEP), and 75-95% (cVEP) of each data set. After CI, the number of rejected trials increased (<10 trials). Peak amplitude and latency were extracted at the P1, N1, and P2 components for cAEP and cVEP, and P50 for cSEP across all channels. Components $\times$ 60 channels were entered as ERP features with the group index of either "excellent" or "fair."

Source-Level Feature Set

Forty sources localized for cAEP (P1, N1, and P2), cSEP (P50), and cVEP (P1, N1, and P2) were used as input to the classifier for the source level, based on the source localization using cognitive ERPs validated as being reliably applicable.[19] The inverse problem was solved using exact low-resolution brain electromagnetic tomography (eLORETA), an advanced version of standardized tomography (sLORETA), which calculates the standardized current source density (CSD, μA.mm^{-2}) at each of the 6239 voxels across the whole brain.[20] The neural sources generated by the scalp-recorded activity were estimated in each component of the auditory, somatosensory, and visual evoked responses. Active sources were defined using the digitized Montreal Neurological Institute 152-space template.[21]

Feature Selection and Classification

To extract the feature set(s) that best discriminated excellent (equivalent to good) from fair CI users, the following aspects were tested: (1) the sensor-level feature set alone (amplitude and latency), (2) the source feature set alone, and (3) the sensor/source combined. To ensure commensurability of the various data types, features were scaled to [0 1]. The Fisher score, a common feature selection method, was used to provide discriminative measures of individual features for classification.[22]

Training was performed using a support vector machine (SVM), which efficiently avoids overfitting in a supervised manner, as evidenced in brain–machine interface applications.[23] Datasets were divided into training and test sets. In order to cross-validate and protect against overfitting, the original dataset was partitioned into 10 folds, and

accuracies were estimated on each fold, using parallel computing in MATLAB (2019b, version 9.4).

Classification Outcome Evaluation

To evaluate classification performance of the feature sets, the following 5 measures were used:

Accuracy: (number of correctly classified "excellent" and "fair" datasets)/(total number of datasets).

Training time: duration in seconds

Sensitivity: (number of correctly classified "excellent" datasets)/(total number of datasets).

Specificity: (number of correctly classified "fair" datasets)/(number of "fair" datasets).

Total misclassification cost: arbitrary units (0-10)

Prediction speed: number of observations per second

Figure 1 illustrates the procedure for machine learning-based classification, based on auditory, tactile, and visual processing cortical activities.

Statistical testing was performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA), in-house scripts, and built-in functions in MATLAB with the Optimization and Statistics Toolboxes (2014a, 2019b, Mathworks, Inc., Natick, MA, USA). A $P < .05$ was considered statistically significant; 95% confidence intervals were also calculated. Data were presented as means $\pm$ standard deviations; outliers were defined as values that differed from the mean by $\pm$ 2 standard deviations.

RESULTS

Fourteen sequential EEG recordings were included in the current analysis. Table 1 provides demographic details and Table 2 summarizes the dataset characteristics. As shown in Figure 2, the initial comparison resulted in the highest classification accuracy by the tactile combined-level feature set, followed by the visual combined-level and tactile source-level feature sets.

As summarized in Table 3, mean classification accuracies by the sensor level were 76.58 $\pm$ 12.47%, 58.66 $\pm$ 23.83%, and 79.94 $\pm$ 11.18% in the auditory, tactile, and visual conditions, respectively. Mean classification accuracies by the source level were 65.43 $\pm$ 11.86%, 95.5 $\pm$ 4.22%, and 79.98 $\pm$ 4.07% in the auditory, tactile, and visual conditions, respectively. Mean classification accuracies by the combined-level were 82.71 $\pm$ 2.80%, 98.88 $\pm$ 2.57%, and 93.5 $\pm$ 4.89% in the auditory, tactile, and visual conditions, respectively.

Classification by level significantly differed among the 3 conditions ($F = 28.563$, $P = .000$); multiple comparisons by Bonferroni corrected post hoc test showed no significant difference between sensor and source levels ($P = .623$), whereas they showed significant differences between sensor and combined levels ($P = .000$), as well as source and combined levels ($P = .029$). Classification by modality significantly differed among the 3 domains ($F = 8.403$, $P = .000$); multiple
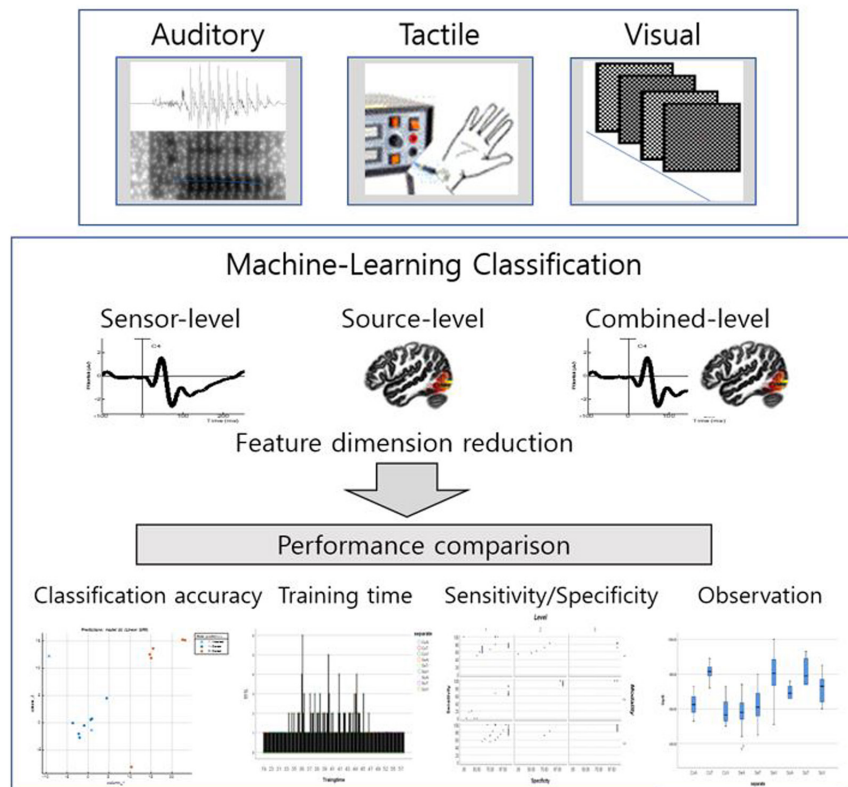
Figure 1. Procedure for extracting factors that best predict cochlear implantation outcomes. From auditory, tactile and visual stimulation, sensor-level, source-level or combined-level features were extracted as an input for machine-learning classification. Using a t-test ($P < .01$), dimension of the features was reduced for computational efficiency. Performances among features were compared based on classification accuracy (%), sensitivity/specificity, training time and observation speed.

comparisons showed no significant difference between auditory and tactile modalities ($P=.178$), whereas they showed significant differences between auditory and visual modalities ($P=.029$), as well as between tactile and visual modalities ($P=.000$). Sensor-level classification tended to yield higher accuracies in the auditory and visual than in the tactile condition, but the difference was not statistically significant.

Training time was shortest in the auditory source-level method (0.33 ± 0.08 s), followed by the visual source-level method (0.36 ± 0.06 s). Training time was longest for classification with the tactile combined-level method (0.51 ± 0.09 s), followed by the auditory combined-level method (0.50 ± 0.07 s).

Figure 3 summarizes the performance of the 4 measures. The analysis of variance result was not statistically significant for sensitivity ($F=1.182, P=.395$) or modality ($F=0.174, P=.846$), but was significant for the level × modality interaction ($F=31.275, P=.000$). Sensitivity

was highest in the tactile combined-level method (99.99%), but was not significantly different from the visual combined-level method (89.17%), as shown in Figure 3A.

In Figure 3B, the level effect for specificity was marginally significant ($F=6.840, P=.051$), but the modality effect was not statistically significant ($F=1.314, P=.351$). The interaction between level and modality was significant ($F=8.049, P=.000$). The auditory and visual combined-level methods showed the highest specificity (99.99%), followed by the tactile combined-level method (98.15%). The tactile source-level method exhibited relatively high specificity (97.78%), compared to other conditions (54.33-84.12%).

In Figure 3C, the effects of total misclassification cost, indicated by arbitrary units (0-10), as well as prediction speed and training time, yielded non-statistically significant findings for both level and modality, but the interaction was significant ($F=17.007, P=.000$, $F=48.565$, $P=.000$, $F=8.531, P=.000$). The tactile combined-level method had the lowest classification error (*i.u.* 0.17 ± 0.38), followed by the tactile

Table 1. Demographic Details of the Participants

Cohort	P01	P02	P03	P04
Sex (M/F)	M	F	M	M
Deafness duration (years)	20	20	17	19
Age at CI (years)	33	31	36	59
Device	Cochlear/CI422	Cochlear/CI422	MEDEL/Concerto	MEDEL/Concerto
CI ear	Right	Left	Right	Right

Table 2. Summary of the Dataset Characteristics

Dataset ID	CI Side	Time Point	SRS (%)	Performance Group[*]
1	Rt	Pre-op	20	2
2	Rt	M3	70	2
3	Rt	M6	85	1
4	Rt	M12	90	1
5	Rt	M18	95	1
6	Lt	Pre-op	10	2
7	Lt	M3	45	2
8	Lt	M6	55	2
9	Lt	M12	65	2
10	Lt	M18	75	1
11	Rt	Pre-op	10	2
12	Rt	M6	65	2
13	Rt	M12	75	1
14	Lt	Pre-op	20	2

SRS, speech recognition score. *Performance group definitions were based on a cutoff threshold of 70%: group 1 was assigned when SRS was > 70% and group 2 was assigned when SRS was ≤ 70%. Lt, left; Rt, right; Pre-op, pre-operation; M3, 6, 12, 18; follow-up at 3, 6, 12, and 18 months after cochlear implantation.

Classification accuracy (%)
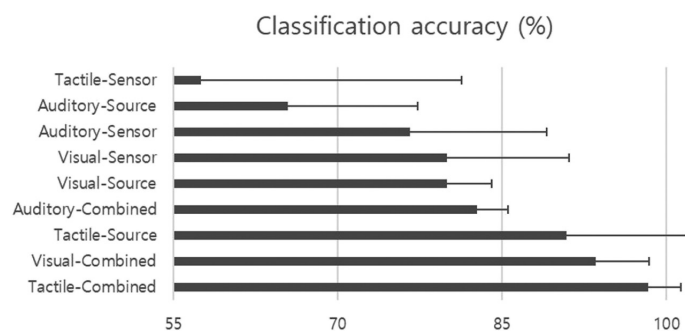
Figure 2. Classification accuracies of individual feature set. Error bars indicate standard deviations.

source-level method (*i.u.* 0.60 ± 0.55); the tactile sensor-level method exhibited the worst total misclassification cost (*i.u.* 4.55 ± 2.62), followed by the auditory source-level method (*i.u.* 3.80 ± 1.30). The number of observations was the largest in the tactile source-level method (818.00 ± 87.58/s), followed by the tactile combined-level method (810.56 ± 44.65/s). The number of observations was the smallest in the visual combined-level method (582.00 ± 64.53/s), followed by the auditory sensor-level method (585.75 ± 67.67/s), as shown in Figure 3D.

Table 3. Descriptive Statistics of Classification Accuracy Depending on Modality and Feature Level

	Auditory	Tactile	Visual	F	P
Sensor[a]	76.58 (12.47)	58.66 (23.83)	79.94 (11.18)		
Source[b]	65.42 (11.86)	95.50 (4.22)	79.98 (4.07)		
Combined[c]	82.71 (2.80)	98.88 (2.57)	93.50 (4.89)	8.043***	.000

*Mean (SD), Post hoc Bonferroni, a, b < c, ***P < .001.

DISCUSSION

We demonstrated that the tactile response in the brain provides a powerful predictive factor for current speech recognition ability in cochlear implant users. This finding is consistent with the results of a previous report regarding the association between speech and perception after CI and cSEP, which indicates cross-modal reorganization by the somatosensory modality in children who have undergone CI. Tactile stimulation activates the auditory cortical regions in children who have undergone CI, in contrast to children with normal hearing; this provides information regarding expected patterns of cSEPs and current density reconstruction involving postcentral cortices, contralateral to the side of tactile stimulation.[24]

Our investigation was based on the assumption of cross-modal reorganization due to deafness, as well as the possibility of functional reversal by electrical stimulation. Functional compensation following a specific sensory loss might lead to development of a capacity that exceeds normal function, as observed in the somatosensory re-organization in congenitally deaf adults[25] and in the auditory/somatosensory re-organization in patients with blindness.[26]

We achieved 98.3% of maximum classification accuracy with the tactile feature set. Our results demonstrate that the combined use of sensor-level and source-level feature sets significantly improved the classification accuracy from fair to excellent after CI. The combined use of sensor-level and source-level feature sets is presumed to provide improved classification accuracy, as evidenced by the percentages of each feature type; sensor-level only (23%), source-level only (64%), and more than 2 (7%), reviewed in 2007-2011 publications.[27]

We observed that overall somatosensory activation was obvious 3 months after CI in a patient (A, defined as an excellent performer at this time point); conversely, another patient (B, a fair/poor performer at this time point) exhibited additional activation in non-somatosensory regions, such as auditory and frontal areas. This pattern was dramatically modified in patient B after a year, while patient A underwent gradual changes to a higher proportion of somatosensory activation. Our result might support the enhancement in speech recognition by both electro-tactile and electro-auditory stimulations, in which tactile vibrating patterns converted from voice pitch might entrain incorporated auditory and tactile brain regions properly and thus improve discrimination of speech intonation contrasts.[28]

In the current study, auditory re-organization in the brain was shown as a non-primary factor in successful classification of CI outcomes, specifically in our adult data, in contrast to observations such as the reversal of normal tonotopy representation in cochlear implant users of >3 months.[29] We used the same /ba/ sound to elicit ERP responses, in accordance with the approach used by Sharma et al.; their study revealed modifications in the ERP waveform at 14 months after CI, as well as current density reconstruction at 27 months after CI.[12]

We also found that functional reversal in the visual domain was a powerful predictive factor, followed by the tactile domain, when classified with combined feature sets. We chose the pattern reversal paradigm to elicit cVEPs based on previous literature that preferred the use of pattern reversal cVEPs to obtain estimates regarding
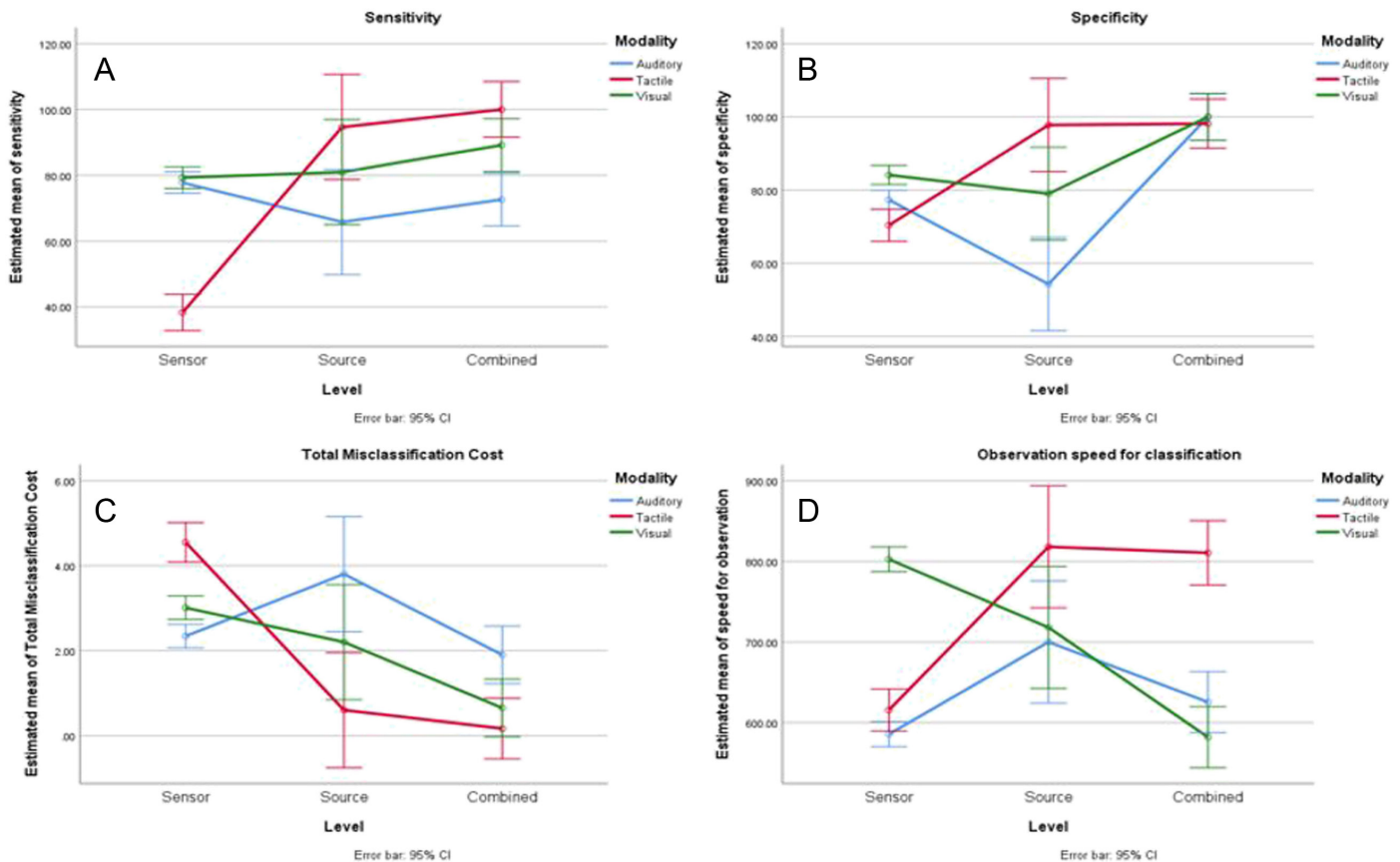
Figure 3. Estimated means of sensitivity (A), specificity (B), total misclassification cost (C) and observation per second (D) in sensor, source and combined classification features across modality of auditory, tactile and visual domain. Error bars indicate 95 % confidence interval.

form sensing with edges; thus, visual acuity is less variable in terms of waveform and timing.[30] cVEP is dependent on age; however, our patients were not affected (all were 30-50 years of age). Taken together, tactile activity in the brain is presumably optimal for prediction of CI outcome in terms of accuracy, sensitivity, total misclassification cost, and observation speed.

The limitations of our study include the small sample size and the uncontrolled CI site. Nevertheless, longitudinal observations enabled us to partially compensate for the small number of patients by providing different time points with differing outcome statuses. In the current study, we only focused on sensor-level, source-level, and combined-level classifications; however, connectivity around the main auditory and language regions should be further investigated in future studies, as electrical stimulation after CI may have caused changes in functional network characteristics.

Ethics Committee Approval: Institutional Review Board (IRB) of Seoul National University Hospital (No. 1701-005-819).

Informed Consent: Participants provided informed written consent after the detailed explanation of the study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept – J.K., M.S., J.H., M.P., J.L. ; Design – J.K., J.L.; Supervision – M.S., M.P., S.O., J.L.; Resource – J.K., M.S., J.L.; Materials J.K., M.S.,

J.H., M.P., T.N., S.O., J.L.; Data Collection and/or Processing - J.K., M.S., J.H., T.N., S.O., J.L.; Analysis and/or Interpretation - J.K., M.S., S.O., J.L.; Literature Search - J.K., M.S., J.H., M.P., T.N., J.L.; Writing - J.K., M.S., J.H., M.P., T.N., S.O., J.L.; Critical Reviews - J.K., M.S., J.H., M.P., T.N., S.O., J.L.

Conflict of Interest: The authors have no conflict of interest to declare.

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