CHAPTER 6: DISCUSSION

Behavioural responses are sufficient to obtain optimal threshold and comfort levels for programming majority of post-lingual adult cochlear implantees. Although these levels are reasonably accurate at the time of programming, the threshold and comfort levels tend to change over time and hence sequential re-programming of the Maps based on behavioural responses is necessary as and when required (Abbas et al, 2000; Brown et al, 2003; Gordon et al, 2004). On the contrary, establishing accurate behavioural thresholds and comfort levels is extremely challenging for very young children and those with syndromes / multiple disabilities, in whom identifying consistent behavioural responses to electrical stimuli, is often a daunting task. Hence, the behavioural observation technique used in infants and toddlers for implant programming is likely to over-estimate threshold measures, when compared with procedures used in older children that use conditioned responses (Gordon et al, 2004). Programming very young children is clinically challenging even for very experienced audiologists at times. Hence, in the present day various electrophysiological tests have taken precedence in the programming of such ‘Difficult to MAP’ individuals.

Suspicion of a disparity between the electrophysiological thresholds and the behavioural parameters, needs to be thought of as one of the reasons, when a cochlear implantees’ performance is not up to expectations, as
diagnosed by their poor auditory-verbal skills and general behavior to implant usage. A multitude of electrophysiological tests are clinically available today, to provide a helping hand for confirming the integrity of the implant in such cases. Intra-operatively and post-operatively EABR, ESRT and ECAP measurements can be used to assess the device integrity and to measure amplitude growth function of the nerve response (Mason, 2004). Such objective data help in sequentially programming the device and can also be used as possible predictors of implant performance over time (Brown et al, 2000).

Although all implant manufacturers provide commercially available standardized testing modules for performing electrophysiological tests like ECAP, ESRT & EABR along with their programming software, they do not stress the necessity for performing these tests as a routine in order to program the implant. By & large, these tests have been used for trouble-shooting and for research purposes. In newer software, there is an option of importing ECAP thresholds into the Mapping module, for optimal setting of current levels. But many a times, a single objective measurement like the ECAP may not necessarily correlate and predict the behavioural levels accurately (Gordon et al, 2004). This may be due to the inherent differences in the pulse width and stimulation rate, which exist between the electrical response of the auditory nerve recorded as a compound action potential and the actual behavioural response to a stimulus which is used to program the implantee (Gordon et al, 2004; Kreft HA et al, 2004; Basta et al, 2007; Davids T et al, 2008).
Gordon, in 2004, stated that electrophysiological thresholds might be useful (when behavioural responses are questionable) to provide young children using cochlear implants with audible and comfortable auditory inputs, from which they can learn to detect sounds. Once they detect the auditory stimulation provided, these children begin to learn & respond consistently to discrete stimulus presentations. As this ability improves, reliable behavioural stimulation levels are obtained. This author emphasized that behavioural measures of threshold remain the gold standard of setting minimum stimulation levels. This principle is being followed in the Cochlear Nucleus Implant system, which uses a threshold level based programming technique. However, this author also concluded that current clinical techniques may not be the best methods for determining maximum stimulation levels.

This aspect of her observation, induced interest in the present study, since identifying the most comfortable levels seems to be the pivotal factor, in order to program a ‘Difficult to MAP’ child, using the MedEl or Advanced Bionics Implant systems (which use a comfort level based programming technique). Hence, the present study focused on utilizing objective measures to predict optimal comfort levels for cohorts of comparable cochlear implantees, using the various devices from the three implant companies.

Literature has documented comparisons between the intra-operative and post-operative electrophysiological responses of the auditory nerve
(Abbas et al, 2000; Hill K et al, 2004 and Mason S, 2004). Many research papers conclude that there is a definite variation in the current levels, which may be attributed to factors like wound healing with reduction in the neural tissue - electrode interface, alteration of the electro-chemical gradient within the cochlea, neural re-organization within the cochlea and adaptation of the auditory nerve to become more conducive for electrical stimulation over time (Brown, 2003; Gordon, 2004; Basta, 2007 and Thai-Van, 2001). It is believed that impedance to current passage reduces in due course of time and synchronous firing for electrical stimuli via the implant sets in. The higher auditory centers also get receptive and fine-tuned for stimulation through the cochlear implant, with implant usage.

Hence, post-operative electrophysiological tests are more efficient in predicting the Mapping levels, rather than relying upon intra-operative measures (Gordon, 2004; Stephan, 2000; Thai-Van, 2001). Hence, this research work did not take intra-operative electrophysiological parameters into consideration for predicting optimal MAPs, but was focused on exploring the relationship between post-operative electrophysiological tests and behavioural levels, from the time of ‘Switch-On’ of the device, through the period of habilitation for the next one year.

The most popular & commonly used electrophysiological test in the intra-operative scenario & in the post-operative period is the ECAP
measurement. ECAPs can be used to determine the amount of surviving neural tissue along the length of the electrode array and also to determine psychophysical information used in cochlear implant fitting, but not to predict performance of the device (Abbas, 2000; Brown, 2003; Shpak, 2004). Assessment of a cochlear implantees' functional outcomes and performance depends on a multitude of factors like the age at implantation, etiology and duration of hearing loss, pre-amplification history, cognition, intellect, patient motivation for implant use and the effectiveness of auditory verbal habilitation (Shallop JK, 1995; Waltzman SB, 2002; Gordon, 2004).

It is established that ECAP thresholds fall in-between the threshold and comfort levels, within the dynamic range of the MAPs and significantly correlate with both threshold and comfort levels (more so with the threshold levels), but raw ECAP data alone is not adequate for estimation of absolute Mapping levels in implantees (Almqvist B et al, 1998; Dillier N et al, 2002; Cohen LT et al, 2003). Hence, correction factors have been suggested for ECAPs to be of any predictive value. A number of investigators have described various methods with correction factors and yet there does not seem to be a universal approach for calculation of the predicted MAP values from the ECAPs alone (Abbas, 2000; Kiefer J, 2001; Thai-Van, 2001; Franck KH & Norton SJ, 2001; Smoorenburg, 2002; Di Nardo, 2003; Craddock, 2004; Kaplan-Neeman, 2004; Lai W, 2004; Han, 2005; Caner, 2007, Holstad BA, 2009; Alvarez I, 2010 and Mckay CM, 2013). Whilst, behavioural
thresholds correlate well with ECAPs over groups, significant differences may still occur between ECAPs and behavioural measurements individually among subjects of the study group, as also displayed among candidates in the various cohorts of this research work. The general consensus today is that ECAPs when used alone, is not a very precise & sensitive tool for objectively predicting Mapping parameters (Miller CA et al, 2003; Gordon et al, 2004).

A study by Thai-Van et al, in 2001 suggests that the correlation between the neural response threshold and behavioural threshold levels may improve from the base towards the apex of the cochlea. However, a significant correlation can be demonstrated for all tested electrodes at 12 months post-implantation. During the first months, care must be exercised when interpreting neural response telemetry measurements, as a positive test does not necessarily mean that the stimulus delivered to the acoustic nerve will be centrally processed with the result of an auditory perception.

Abbas & Hughes, in 2001 revealed chronological changes in NRT over time from the day of surgery. Statistically significant changes in the NRT thresholds of children were observed until 3 to 8 months following initial stimulation. Measures of NRT slope in children did not stabilize until 12-months post-implantation and longitudinal trends in NRT measures mirrored the threshold levels more closely than comfort levels. Smoorenburg, in 2002 concluded that NRT thresholds, have a positive correlation with comfort levels,
but cannot be used to predict the overall comfort levels and tilt of the comfort profile, since prediction of the slope of the maximum stimulation curve, which is the most critical factor in speech perception, from the NRT thresholds was poor. In the present study, ECAP measurements showed moderate correlations with comfort levels over time. There were wide differences between the NRT based predicted levels and behavioural comfort levels across the array, with a range of 6 to 110 Programming Units noted between subjects. There were inter-electrode and inter-patient variations between the ECAP predicted levels and behavioural comfort levels over time. The above observations suggest that ECAP based correlation when used alone is not a useful method for predicting behavioural comfort levels.

Investigators have assessed the efficacy of ESRT in predicting comfort levels for optimal programming and they found ESRT to be of greater predictive value than ECAP for estimation of behavioural comfort levels (Gordon et al, 2004; Han et al, 2005; Caner et al, 2007). Postoperative ESRT thresholds fall close to the comfort levels in a MAP, show high correlations with behaviourally obtained comfort levels and help predict the maximum comfort level pattern across electrodes (Jerger J et al, 1988; Stephan K, 2000; Bresnihan M, 2001; Walkowiak A, 2010). Fitting the speech processor based on ESRT data has been shown to result in speech perception scores equal to or better than those achieved with conventional fitting techniques (Shallop JK, 1995; Zehnder A, 1999; Almqvist, 2000; Sasidharan P, 2013). But, especially
among very young children, initial fitting measures with ESRT alone has not been very successful due the inherent nature of ESRT thresholds to overestimate the comfort levels, which may result in the setting of too loud a MAP in such children, thereby inducing an aversion for implant use among these children (Walkowiak A, 2010).

Spivak & Chute, in 1994 stated that an increase in behavioural comfort levels over time, suggested that children using cochlear implants become more willing and able to tolerate higher stimulation over time and that the clinician who programs their implants attempted to foster this increased tolerance. They found that, like comfort levels, ESRT thresholds also raised over the first year of implant use and the increased tolerance to higher levels of stimulation shown by increasing comfort levels and ESRT over time was possibly due to changes in the conditioning of the auditory nerve and lower brain stem. Thus, an expanded dynamic range emerges over time and this may suggest a change in neural response with increasing stimulus level, with on-going implant use. Hence, accurate estimation of comfort levels and loudness balancing are of greater value than setting behavioural threshold levels, while programming young children.

In the present study, the overall ESRT correlations with comfort levels were found to be better than ECAP correlations across the array which persisted over time. ESRT based predicted comfort levels recorded among the
study group, fell more close to their actual behavioural comfort levels, than the 
ECAP based predicted comfort levels, with a difference of 4 to 34 
programming units noted in most cases, among the various cohorts. Thus, it is 
inferrered that the ESRT based prediction method may be more useful than the 
ECAP based prediction method, when used alone.

Authors have found that EABR thresholds correlate well with 
behavioural thresholds similar to ECAPs and they provide a sensitive & 
effective technique to comprehensively test implant function by assessing 
nearal survival along the cochlea & integrity of the auditory pathway up to 
brainstem level (Truy E et al, 1998; Abbas PJ et al, 2000; Miller CA et al, 2000; 
Brown CJ et al, 2003; Gordon et al, 2004). EABR has been the gold-standard 
tool for meticulous analysis of individual electrodes along the array, to identify 
non-auditory electrodes and confirm device failures. In a poor CI user, EABR 
helps to identify & redefine erroneous maps which may exist undiagnosed 
even by ECAP measurements (Shallop JK et al, 1991; Gordon et al, 2004). 
The possible reasons for EABRs not being widely used in clinical practice 
today, is that it requires a cumbersome set up, is time-consuming, needs 
expertise and a fully cooperative / sedated patient.

In the present study, it was observed that most EABR thresholds fell 
below their respective most comfortable levels (more so in the apical array), 
and within the dynamic range of the behavioural MAPs, except for a few EABR
measurements, which over-shot their comfort levels, especially in the basal array regions. By and large, the EABR correlations with comfort levels among the various cohorts were found to be comparable to their ESRT correlations, respectively. EABR based predicted values for comfort levels were close to the actual behavioural comfort levels, with a difference ranging between 3 to 28 programming units across the array, in the various cohorts. The differences were more pronounced in the apical array, while the differences were lesser in the basal array. This finding suggests that EABR based prediction method when used alone, may be useful to predict comfort levels more towards the basal array, rather than in the apex of the cochlea, but the research team believes that a further in-depth study in a larger sample is necessary, in order to arrive at such a conclusion.

Gordon’s study in 2004 showed that ECAP and EABR amplitudes increase over the first year of implant use in children and their wave latencies and inter-latencies decreased over time. These findings may reflect improvements in neural conduction velocity and neural synchrony, which could also affect the way in which the central auditory system codes changes in the intensity of electrical stimulation. Gordon also described the fact that threshold levels from non-behavioural objective measures did not change over time, whereas behavioural levels of threshold decreased, since children experienced a gradual increase in awareness to auditory input through the implant, rather than improvements in auditory sensitivity at the level of the
auditory nerve or brain stem. Decreasing threshold levels over time could be a reflection of increased reliability in behavioural measures as the child becomes more experienced in listening for auditory input through the cochlear implant and the clinician grows more confident in the child's responses with repeated measures of the test over time.

Subsequent literature suggests that correction factors based on all available electrophysiological measures like ECAP, ESRT & EABR thresholds are needed to predict behavioural stimulation levels required for programming in difficult situations (Han et al 2005; Caner et al 2007; Van Den Abbeele T et al, 2012). Various methods have been described for applying objective measures to predict behavioural levels in ‘Difficult to MAP’ cochlear implantees.

In the past, correction factors proposed to predict threshold and comfort levels from objective measures were based on the difference between objective thresholds and at least one behavioural measure (Abbas & Hughes, 2000 & 2001; Zimmerling & Hochmair, 2002). These studies suggested extrapolation of this average value across the rest of the array in order to set behavioural levels. But, this technique was inconsistent and not foolproof, since there were variations in behavioural levels between the apical and basal array electrodes. Changes in objective and behavioural responses with respect to the electrode location and over time with ongoing implant use, imply
that such correction factors do not remain static at all times. Correction factors may need to be adjusted with increased cochlear implant experience to account for increased awareness and experience with auditory inputs (Abbas et al., 2001; Di Nardo et al., 2003).

Brown et al, in 2003 described a calculation based on comparison of NRT and behavioural responses from a single, medial electrode. This correction factor was applied to each electrode for which an NRT was recorded. C and T levels on electrodes for which an NRT response was not recorded were interpolated, based on mapping levels from adjacent electrodes. This author noted a strong correlation between NRT and behavioural measures in adults, reporting a coefficient ‘r’ value of 0.83 between NRT threshold and T level and 0.77 between NRT threshold and C level. Subsequent studies suggested that correction factors should be made for at least one apical and mid-array electrode, and taking into account the age of the child, may have to be revised again during the first year of implant use (Gordon, 2004; Basta, 2007).

It is a known fact that all electrodes along the array do not respond to stimulation in the same way. Apical electrodes may have significantly lower thresholds when measured by ESRT, ECAP, EABR and behavioural measures than the basal electrodes. Gordon et al, 2004, studied this interesting phenomenon by dividing the electrode array into three offsets –
apical array, mid-array and basal array, wherein a correction factor was created based on the difference between the objective threshold and behavioural level for a representative electrode in each offset across the array. Gordon found a tendency toward increased differences over time in the apical electrode and mid-array, while less significant increases in the basal electrode differences over time. She also proposed that ECAP and ESRT can be used independently in Cochlear Nucleus implantees, to predict minimum and maximum stimulation levels, respectively, and thus optimize the dynamic range along the electrode array.

This suggestion has not been put much into clinical use in the Cochlear Nucleus implantees, since the two electrophysiological parameters described were not correlated with a single behavioural measurement and in ‘Difficult to MAP’ scenarios acquiring both threshold and comfort levels (two variables on a single electrode) consistently for any electrode across the array, in order to predict optimal behavioural levels, appears more confusing and doubles the task of the implant audiologist. Further literature for clinically applying this method of prediction, is currently not available, to the best of knowledge of the research team.

In order to overcome any inherent differences in current levels, observed while using a single measurement like ECAP or ESRT for predicting Mapping threshold / comfort levels, the present study hypothesized the use of
a multi-modal technique with three objective measures (ESRT, EABR & ECAP), which together may correlate and predict behavioural levels better. Hence, the present study has taken the concept proposed by Gordon, a step further by the creation of independent correction factors, based on multiple regression models developed individually for the three offsets across the electrode array (Apical array, Mid-array & Basal Array).

This method focuses on deriving optimal comfort levels (a single, dependant variable), based on its multi-modal correlations with three objective measurements (three independent variables), generated at three locations across the electrode array. The research team has followed a model of three offsets across the array, similar to Gordon’s method, while using this multi-modal technique, for predicting comfort levels based on the linear and multiple regression methods, since this would provide at least three optimal predicted comfort levels across the array, which will be of vital use to begin programming if behavioural levels are unknown.

Results from the present study have shown that such statistically predicted comfort levels were found to be in proximity to the actual behavioural comfort levels recorded among the cohorts and they were statistically reliable. This multi-modal statistical prediction method was found to be successful, when practically applied in the clinical scenario among randomly selected candidates of the various study groups.
The multi-modal test method performed in the present study, which used three objective electrophysiological parameters, improved the correlations with the behavioural comfort levels and also the accuracy of prediction to an extent, higher than the individual prediction methods. In some subjects, the accuracy was as close to less than 2 programming units, which was not observed while using the various linear regression methods; while in other subjects the difference in values ranged between 3 to 29 programming units, across the array which was comparable to the individual prediction methods.

Thus the authors of this research work, infer that the multi-modal regression method may be more useful than linear regression method for predicting comfort levels, since it shows higher statistical reliability and predictability potential, but its practical application in the clinical scenario, especially in ‘Difficult to MAP’ subjects may not be easy, since it requires good audiological expertise, with more testing time and a cooperative subject.

The clinical efficacy of this multi-modal prediction method among the study groups, has now initiated the research team to further explore its use in various real-life ‘Difficult to MAP’ scenarios. In general, the research team infers that both linear and multiple regression models are good methods for statistically predicting comfort levels. In cases where good correlations occur for all the three measures, a multiple regression would be more beneficial,
since it augments the accuracy of prediction. A judicious selection of measures is mandatory, when a situation is encountered, wherein any of the three measures is not showing a good correlation. In such cases, it will be prudent to opt for two electrophysiological measures for combining into a multi-modal prediction matrix.

The present study, has documented the existence of individual variabilities like the intra-electrode variability over time, inter-electrode variability in a patient or inter-patient variability while comparing electrodes. The study has also revealed the mismatch of few programming units noted across the study group, between the behaviourally measured and statistically predicted comfort levels, while applying the various prediction methods and at the various schedules of testing. This mismatch was pronounced in few subjects, while very minimal in others. This was possibly due to the various factors described below by Hall JW in 2007.

Electrophysiological measurements are performed at default stimulation parameters that are different from the stimulation rates eventually used during cochlear implant programming. Sensitivity and neural reactions recorded to electrophysiological stimuli are bound to be different from the behavioural reactions recorded at higher rates of stimulation, used while programming. The electrophysiological measures from different regions of the cochlea are also bound to be different due to the factors like surviving spiral ganglion...
population, gelling effect of the electrodes to the neural interface and presence of any intra-cochlear fibrosis of scarring due to insertional trauma, impeding the path of current flow. The higher thresholds for electrophysiological responses noted at the basal electrodes were possibly due to the physical current distribution, which required higher current levels in order to evoke a measurable neural activity (Gluckert R, 2005; Roland PS & Wright CG, 2006).

Behavioural response elicited by electrical stimulation with a cochlear implant electrode is understood to be the result of a combination and superposition of the phenomena occurring at three different levels namely, the electrode - tissue impedance with respect to positioning of the electrode contact towards the neural tissue; neural preservation and excitability of the nerve fibers and the cortical / behavioural reactions to the excitation patterns in the higher auditory pathways as influenced by the age at onset of deafness, cognition, intellect, hearing aid usage and duration of hearing deprivation prior to implantation (Sharma A, 2002; Hassanzadeh S, 2002; Zowlan TA, 2004).

All electrophysiological measurements like ECAP, EABR & ESRT objectively record events occurring at the peripheral neuronal levels, yet take no account of the variability present at the higher auditory centers (Hall JW, 2007). It is well known that, behavioural responses are immensely influenced by higher auditory circuits and hence, electrophysiological measurements of the peripheral auditory system alone cannot substitute or replace a
behavioural MAP accurately (Waltzman SB et al, 2002; Psarros C et al, 2010). This practical fact has also been brought out from the results of the various cohorts in the present study.

Behavioural responses to stimulation via the implant vary widely between very young children and older children, wherein factors at the higher auditory level play a major role and there also exist wider inter-personal variabilities between older subjects. This fact is also notable from the results of the present study, which has included implantees whose age ranges from 2 to 12 years. Such a wide range had to be included into the study, at the time of commencement of this research work, in order to acquire adequate number of comparable subjects from both centers of study, who could be grouped together for performing a statistically significant analysis.

This age range, was also necessary due to practical and logistical reasons observed at the two centers of study and also in the Indian scenario, wherein most children received cochlear implants within this age range, due to the financial implications which delay their implantation, even though some of them may have been diagnosed early with profound hearing loss at birth or within one year of age. The study cohorts hence included comparable device-matched subjects with pre-lingual status with an age range of 2 to 12 years. This age range may also have been a vital factor influencing the variability of differences noted between the behavioural and predicted comfort levels, noted
across subjects of the various study groups. This fact further reiterates the hypothesis of the present study, that it is possible to achieve more accurate prediction values by the multi-modal prediction method, if a cohort of comparable subjects who are perfectly age-matched can be chosen for analysis.

The Research Team observed that even though age at implantation may have been an influencing factor on the electrical behaviour of the Auditory nerve, to stimulation via the cochlear implant at Switch-On of the device and during initial fitting, the eventual electrophysiological responses sequentially evoked over a period of implant use, among the subjects with varied ages were not of much clinical or statistical difference, for the purpose of predicting optimal comfort levels.

Hence, the Research Team inferred that electrical (psychophysical) hearing began and progressed in the same way during their one year of follow up, among all the 58 subjects of the study irrespective of their age, implant model or type of speech processor used. In general, an improvement in the accuracy of prediction of comfort levels was also observed over the period of implant usage, which is highlighted by the proximity in the data points, on the scatter-plots of the various cohorts, comparing the actual versus predicted comfort levels, by the time of completion of the study at 1 year of implant use.
Overall, this research work helps to infer that behavioural measures, even if minimally recordable are mandatory to program cochlear implantees and electrophysiological measurements can help as a guideline for programming, but cannot replace or substitute the behavioural levels, comprehensively.

Results have shown that electrophysiological testing is helpful in predicting comfort levels across the array and provides a working MAP at any point of time, when behavioural levels are unknown or minimally available. Data based on correlations and prediction methods as described in this study, may be of reference for implant audiologists attempting similar studies in future.

Performing such multi-modal predictions, gives additional information on the range of the comfort levels and helps in refining / confirming behavioural levels when doubtful. Thus, it is prudent that a combination of objective measures, along with any available behavioural responses should provide the most optimal levels for programming cochlear implants in actual ‘Difficult to MAP’ situations.