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Obligatory CAEP testing in infants – a five year review

Authors: M Golding, H. Dillon, J Seymour, S Purdy, R Katsch

In the year 2000, NAL and the Cooperative Research Centre (CRC) for Cochlear Implants and Hearing Innovation, commenced a series of studies using Cortical Auditory Evoked Potential (CAEP) testing. The overall aim of these studies has been to investigate the potential of using CAEP recordings to demonstrate that speech and tonal stimuli are successfully transmitted through a hearing aid and the auditory system to the level of the auditory cortex in aided hearing-impaired infants.

Since the 1960s, a number of studies have reported the application of this technique in estimating auditory threshold to frequency specific stimuli in adults who were unable to participate in normal behavioural testing (Coles & Mason, 1984; Cone-Wesson & Wunderlich, 2003; Davis, 1965; Hyde, Alberti, Matsumoto, & Yao-Li Li, 1986; Rickards, DeVidi, & McMahon, 1996). A study was also reported at that time where CAEP testing was performed on an infant with brain damage as a means of assessing whether any improvement in the detection of auditory stimuli could be observed when hearing aids were fitted (Rapin & Granziani, 1967). With the discovery of the Auditory Brainstem Response (ABR) (Jewett & Williston, 1971; Purdy et al., submitted), which offered a more stable response than that seen in CAEP testing, studies that used CAEP testing in infants became rare for several decades.

With the implementation of infant hearing screening programs in many parts of the world however, the need to evaluate hearing aid fittings in very young infants has gained increasing importance. NAL has been instrumental in developing a widely-accepted prescriptive method for hearing aid fitting that uses behavioral threshold inputs, or in the case of young infants estimates of behavioural thresholds that are based on electrophysiological thresholds, to derive target gain. In infants that are old enough developmentally to respond reliably to behavioural threshold-seeking techniques (Snik, Neijenhuis, & Hoekstra, 2001) the appropriateness of fit can be established with reasonable certainty but this is not the case for young infants. The recording of CAEPs to speech stimuli has the potential to provide such verification.

Our early experiments conducted with adults as well as infants and young children, investigated the suitability of a range of speech and tonal stimuli, with variable duration and inter-stimulus interval, in evoking clear CAEP responses. While CAEP responses were reliably evoked by an extensive range of supra-threshold speech sounds (male and female voices) and tonal stimuli in infants and adults (Agung, Purdy, McMahon, & Newall, 2006; Purdy et al., submitted) this range of potential test stimuli has now been limited for most experiments to /m/, /g/ and /t/ (female voice). These consonants were extracted from continuous discourse that was spoken by a female with an average Australian accent and filtered using International Long-term Average Speech Spectrum (ILTASS). The stimuli include very little of the vowel transition and were recorded with digitization rates of 44.1 kHz. An additional high-pass filter at 250 Hz was applied to /t/ and /g/ to remove additional unwanted low frequency noise. These essentially vowel-free

stimuli were chosen because they had a spectral emphasis in the low-, mid- and high-frequency regions respectively, as shown in Figure 1, and thus have the potential to give diagnostic information about the perception of speech sounds in different frequency regions.

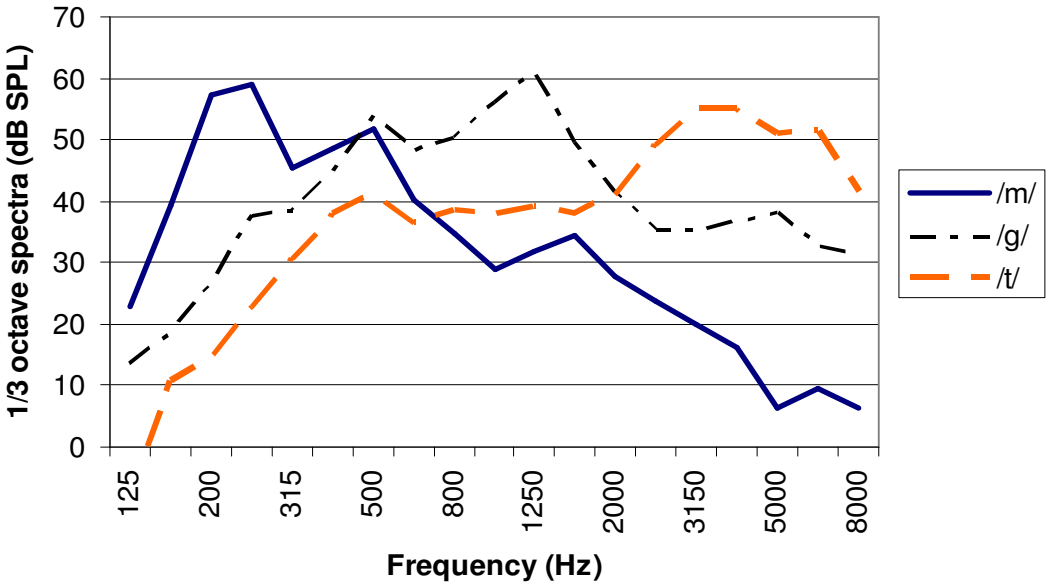

Figure 1: One-third octave spectra for the three speech stimuli (/m/, /g/, /t/) used in CAEP testing.

There are substantial differences in the average infant CAEP compared with adult CAEP waveform. As infants with normal hearing mature, cortical responses change significantly with respect to the shape and latency of the major components over the first 14-16 years of life (Rotteveel et al., 1986; Hyde, 1997; Pasman, Rotteveel, Maassen, & Visco, 1999). The newborn infant CAEP in response to speech stimuli is dominated by a series of positive peaks with a prominent peak at 200 to 300 msec when recorded at the midline (Sharma, Dorman, & Spahr, 2002; Stapells & Kurtsberg, 1991; Kurtzberg, 1989). By adult years (i.e., over 20 years), the dominant component is a negativity (80 – 120 msec)

that is preceded and followed by positive components (i.e., P1 at 50 to 70 msec, and P2 at 150 – 200 msec) (Davis, 1965). These morphological changes with age are likely to reflect underlying developmental changes in the response generators such as improved synaptic efficiency arising from increased axon myelination and maturation of intra and inter-hemispheric connections throughout the cortex (Cunningham, Nicol, Zecker, & Kraus, 2000; Eggermont & Ponton, 2003). Several researchers have examined this latency change as a function of age particularly in normal hearing children and adults or children with cochlear implants but few detail the changes in latency over the first few months of life for normal hearing infants and fewer still examine latency changes in children who wear hearing aids (Cunningham et al., 2000; Sharma et al., 2002; Ponton, Eggermont, Don, Waring, & Masuda, 1996; Pasman et al., 1999; Sharma, Kraus, McGee, & Nicol, 1997). We examined the latency results for the first positive peak (known as P1) in 54 infants, aged 0.2 to 0.75 years, who had normal tympanometry and otoacoustic emissions results and apparently normal hearing. These results are plotted in Figure 2 together with adult latency values and data published by Sharma and colleagues in which the P1 latency for normal hearers and those with cochlear implants is reported (Sharma et al., 2002). The latency of this first positive peak clearly shows rapid decline over the first few months of life.

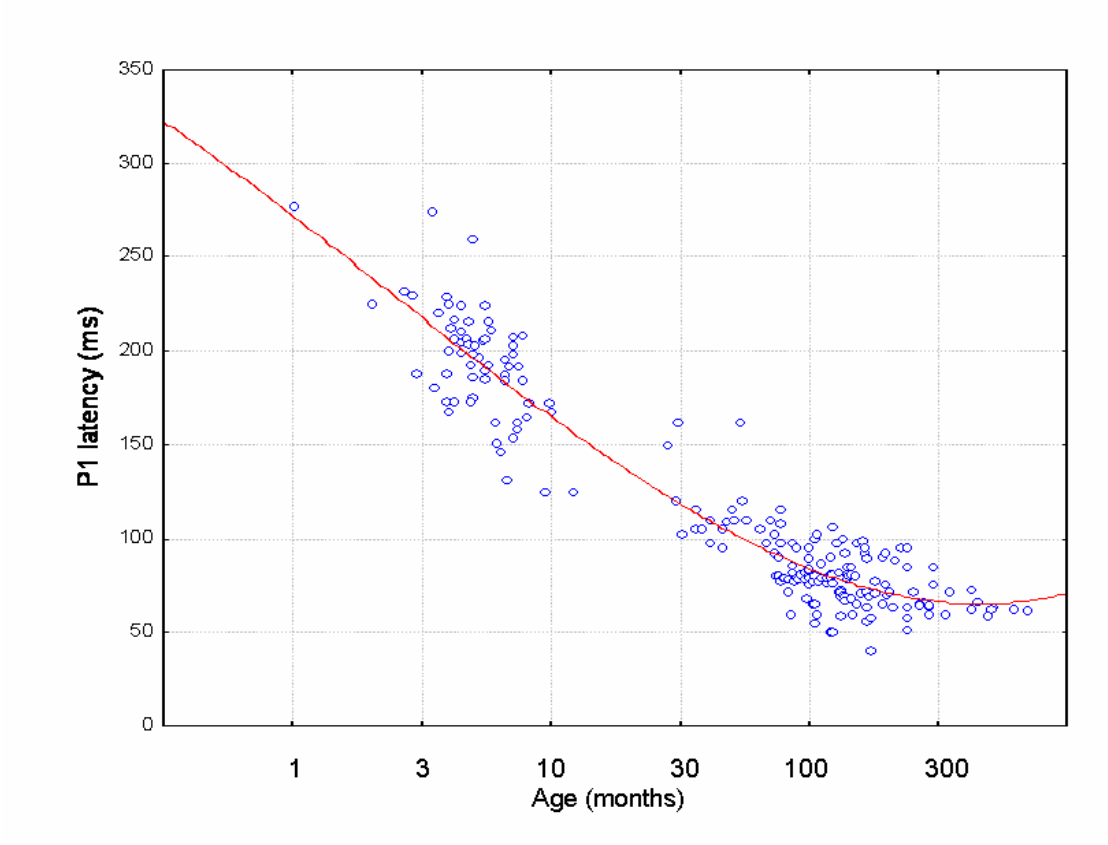

Figure 2: P1 latency as a function of age is shown for normal hearing participants (N = 209).

A number of our studies have investigated CAEP responses in hearing impaired infants and children. In two such studies, CAEP responses were recorded in children with sensorineural hearing loss who were aided to their normal settings. In the first study, CAEPs were elicited 97% of the time when the loss was moderate, and 63-75% of the time, dependent on the stimulus, when the loss was severe. In the second study, speech

stimuli were filtered to four different frequency slopes and the resulting changes to the gain-frequency response produced significant differences in the cortical response for approximately 50% of participants (Purdy, paper in preparation).

Our early experiments relied on latency and amplitude measures to detect cortical responses and these measures were also used to demonstrate that differences existed between cortical responses to differing stimuli (Agung et al., 2006; Purdy et al., submitted). In one such experiment where 20 infants with normal hearing were tested with the three speech stimuli of /m/, /g/ and /t/, large differences were evident in the responses to /t/ versus /m/ for all infants which is consistent with the fact that these stimuli are spectrally and temporally very different (Purdy et al., submitted). Given the variability observed in infant responses, however, (Wunderlich & Cone-Wesson, 2006) and the clinical expertise required to identify a response, the possibility of using a statistical test to detect and differentiate CAEPs has also been investigated. To facilitate this calculation epoched Neuroscan files are exported to MATLAB for analysis. The analysis period consists of 450 points covering the 450 ms period between 50 ms and 500 ms post stimulus onset. The number of sampling points is then reduced by averaging each group of 50 points such that the 450 ms analysis period is reduced to form a "response" condition which contains nine variables. For the purpose of CAEP detection, Hotelling's T^2 (Flury & Riedwyl, 1988; Harris, 2001) is used which calculates the probability that the mean value of any linear combination of the nine variables is significantly different from zero. For the purpose of differentiating between cortical responses, two "response" conditions are formed (i.e., one in response to each stimulus under comparison) and these

two conditions, nine variables and multiple epochs are used as input to a multivariate Analysis of Variance (MANOVA) procedure for analysis. In early trials, MANOVA was also used for CAEP detection where the "response" condition and a second "nil response" condition, which was formed from Gaussian white noise, were used as input to MANOVA. There was however some concern over the potential to violate homogeneity of variance rules across these two conditions and so Hotelling's T^2 has more recently become the statistic of choice for detecting the cortical response.

To assess the validity of using CAEP tests as a tool of hearing aid evaluation, a clinical study was conducted that compared the presence/absence of CAEPs for three speech stimuli with observed auditory behaviours that were recorded using the Parental Evaluation of Aural/Oral Performance in Children (PEACH) questionnaire (Ching and Hill, submitted). The participants were 28 infants and young children who were diagnosed with sensory hearing impairment (N = 15), auditory neuropathy/dys-synchrony (AN) (N = 7), or hearing impairment and multiple disabilities (N = 6) prior to cortical testing. All participants were fitted with hearing aids at the time of testing. It was hypothesized that an increasing number of detected speech stimuli would correlate positively with scores on the PEACH questionnaire. The presence/absence of the cortical response was determined by Hotelling's for 26 out of 28 participants and by a human examiner for 25 out of 28 participants. The mean age-corrected PEACH score and SE are shown as a function of the cortical response in Figure 3 (Hotelling's cortical response) and in Figure 4 (human examiner's cortical response). In both cases, results show an increase in the PEACH score as the number of cortical responses increased. A positive

correlation was found for the detection of corticals and the PEACH outcomes for all children (Hotelling's T^2 (r_s = 0.41; N= 26, p= 0.04); examiner (r_s = 0.45; N=25; p = 0.03)) suggesting that a consistent relationship between cortical and functional outcomes, using both methods of detection, could be demonstrated for these aided infants. In addition, there was reasonably good agreement between the examiner and statistical methods for grading the cortical responses (r_s = 0.65, N = 25; $p < 0.001$).

Case studies of two children with AN, that show how CAEP testing may assist clinicians in management of these cases, have also been reported (Pearce, Golding, & Dillon, 2006; Purdy et al., submitted). These two infants had otoacoustic emissions but lacked ABR responses to tonal stimuli at the time of diagnosis. Figure 5 shows their CAEP responses to one of the three stimuli presented at conversational level. Only one infant (Infant A) had repeatable CAEPs and so in this case, the severity of loss suggested by the ABR outcomes was inaccurate and could have led to over-prescription of hearing aid gain.

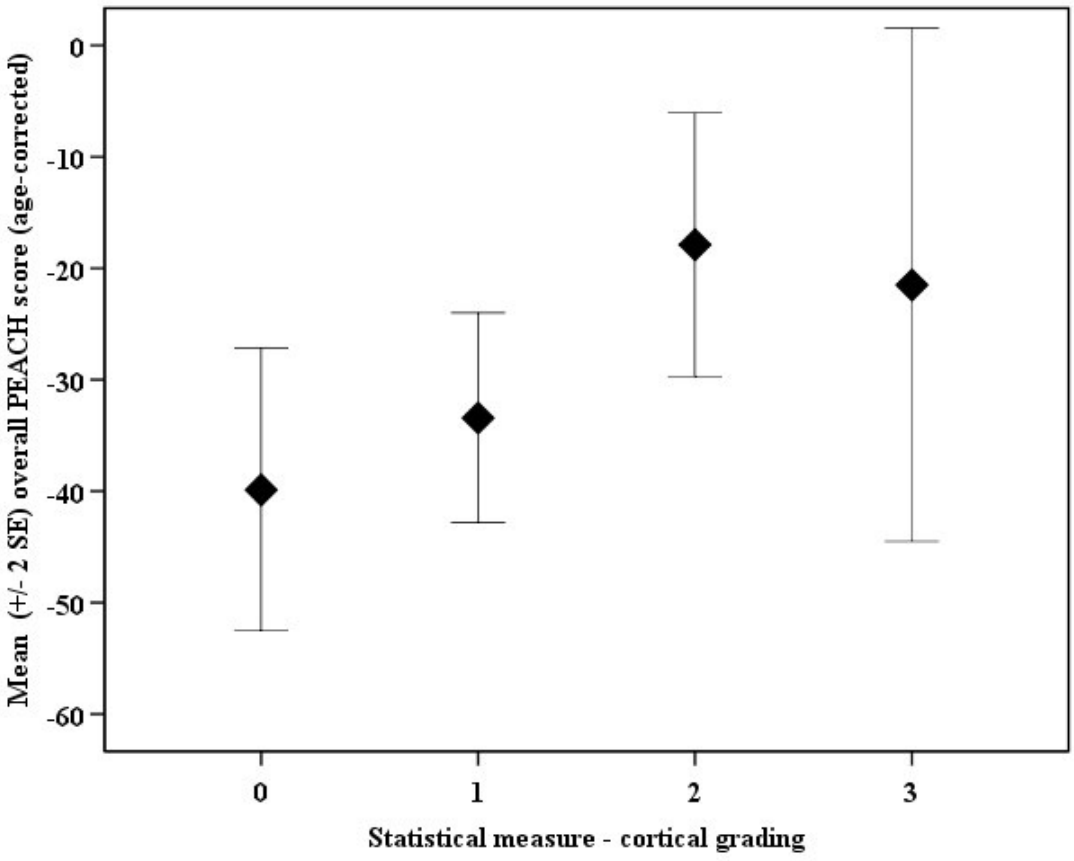

Figure 3: The Hotelling's T^2 cortical grading (where 0 indicates that there were no responses to any of the three speech stimuli and 3 indicates that cortical responses were evident in one or both ears to all three speech stimuli) as a function of the age-corrected PEACH score is shown (N=26).

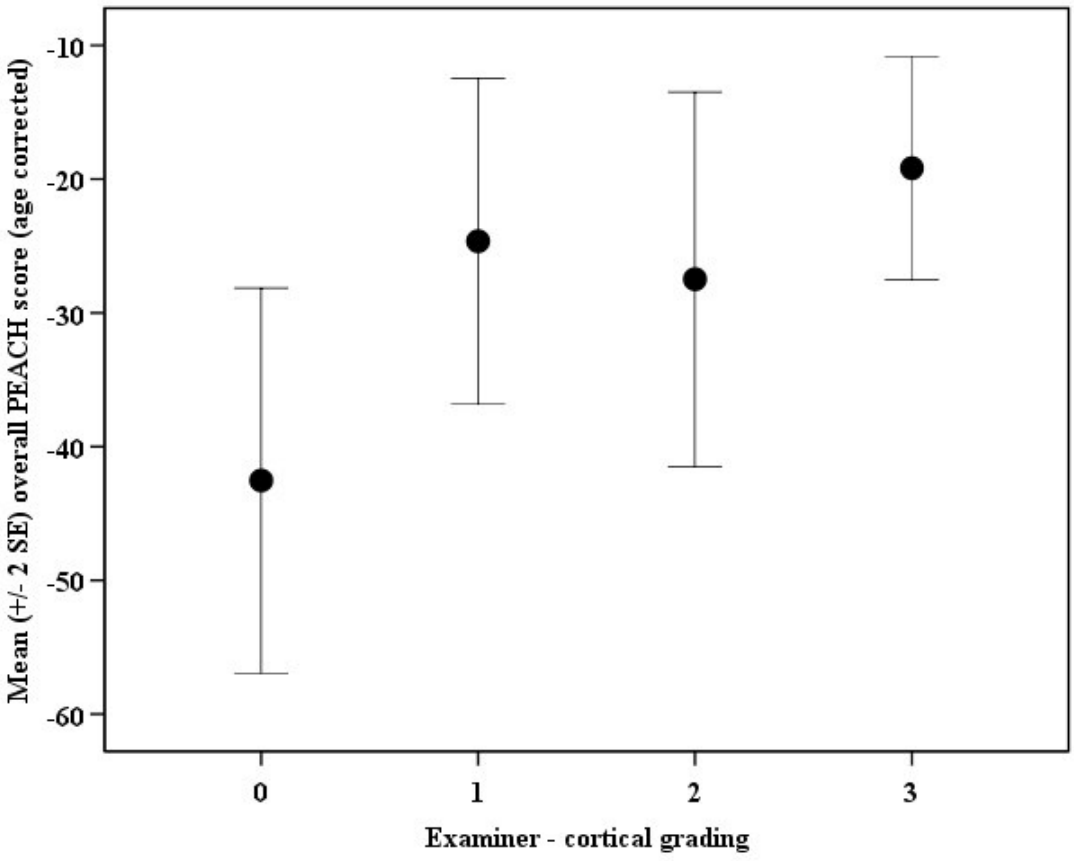

Figure 4: The examiner cortical grading (where 0 indicates that there were no responses to any of the three speech stimuli and 3 indicates that cortical responses were evident in one or both ears to all three speech stimuli) as a function of the age-corrected PEACH score is shown (N=25).

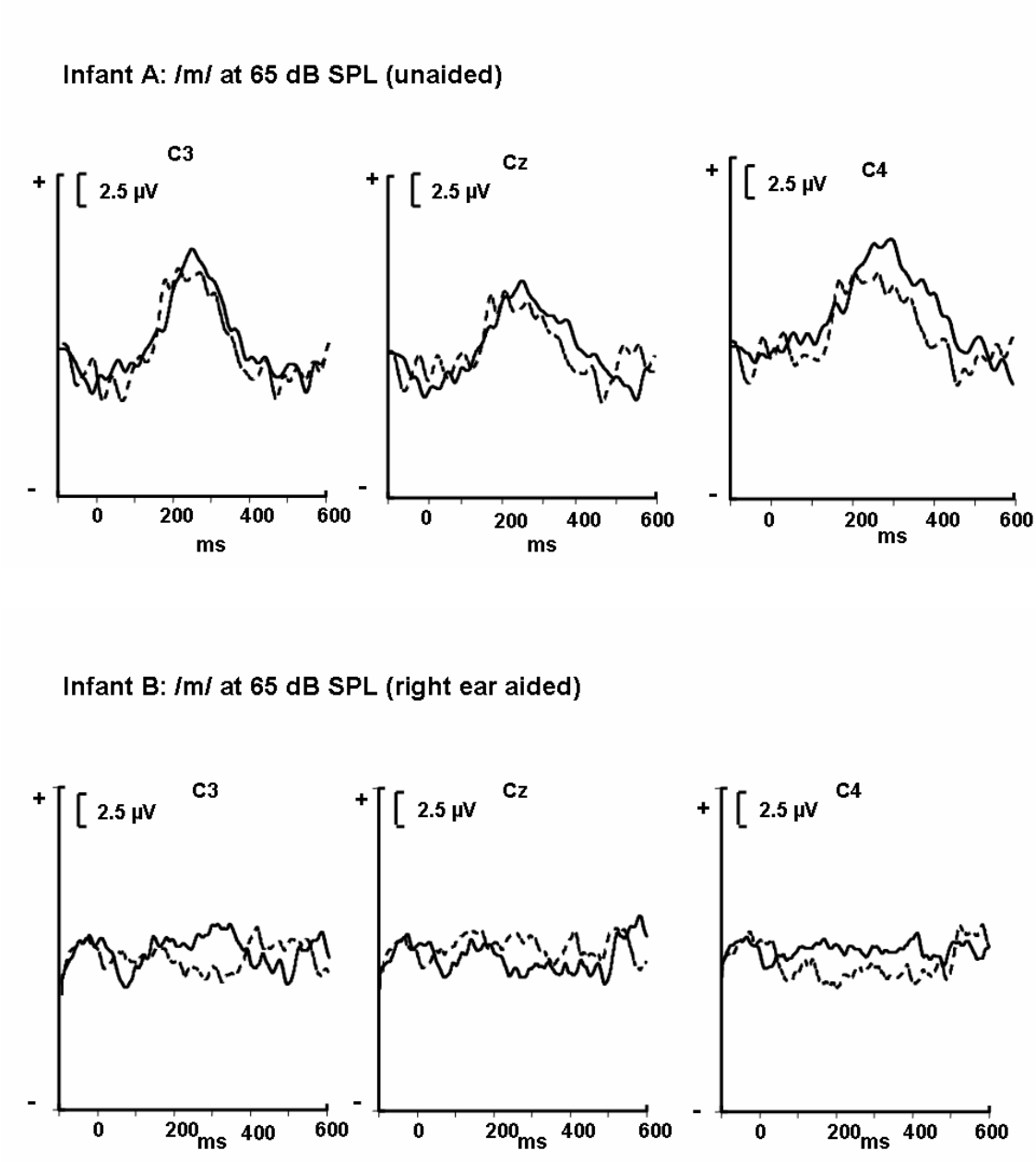

Figure 5: Infant A and B were diagnosed with AN, and had no responses to tonal stimuli on ABR testing. CAEP responses (recorded at 3 electrode sites) to the stimulus /m/ are shown for both infants where the dotted and solid lines represent replicated averaged responses.

The validity of the statistical techniques in the detection of cortical responses has been recently evaluated for adults. Cortical responses from ten adult subjects were recorded to two speech stimuli presented at five sensation levels (relative to their auditory threshold) as well as a non-stimulus condition. Four human experts evaluated the resulting waveforms for the presence of a response and rated their degree of certainty in making their decision. Hotelling's T^2 was also applied to the responses. The sensitivity and specificity of detection was compared for humans and the statistical tests with the latter more accurate in discriminating a cortical response from no response than the expert human observers (Dillon et al, in preparation) (Dillon, Golding, Purdy, & Katsch, 2006). A similar experiment is underway to examine the sensitivity and specificity of these detection methods in infant participants.

Electrophysiological test systems can be expensive and specialized clinical expertise is required to interpret the outcomes in a meaningful way. The CAEP technique, latency/age data and statistical measures of detection and differentiation have been incorporated into Module 1 of the HEARLab system, shown in Figure 6, which is under development as part of the CRC. This portable system, which is designed for clinicians with little experience in cortical testing or statistical interpretation, will make the application of cortical testing far more accessible than is the case at present.

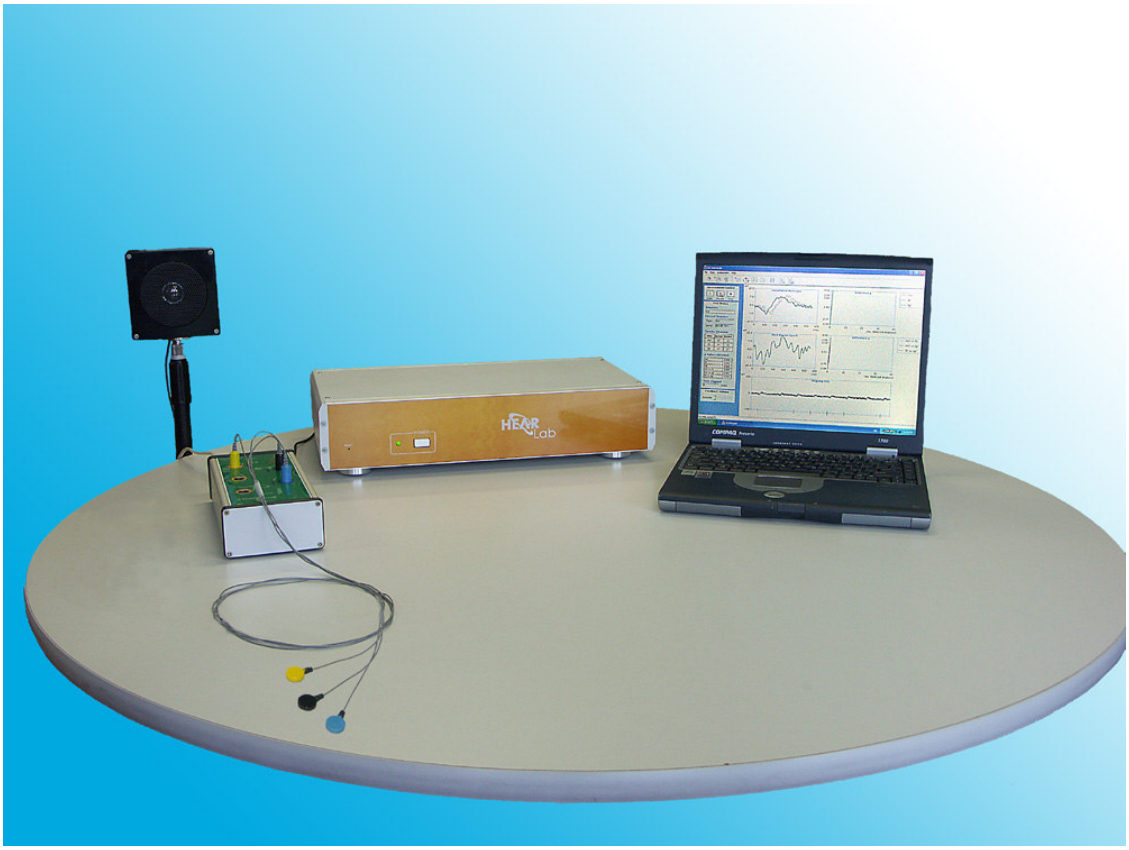

Figure 6: The HEARLab system which performs CAEP testing and result analysis.

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