Peer Commentary on "The Onset and Development of Auditory Function: contributions of evoked potential studies" by Jos J. Eggermont, Ph.D.

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This report provides a good summary of recent findings from studies that have utilized evoked potential measures to examine auditory development. Since ABR can provide an objective and non-invasive measure of functioning and it is relatively unaffected by the infant's state of arousal, its potential utility in infant screening is obvious. Establishing the predictive validity of newborn ABR, however, apparently has proven to be more difficult than anticipated, and the results to date have been somewhat mixed.

Eggermont concludes that newborn ABR in response to clicks (i.e., the I-V interval) will not yield good predictive validity with respect to developmental outcome because maturation of the response is relatively rigid and unaffected by infant health status. By contrast, recent findings in a prospective study by Murray (*Child Development, 1989*) suggest otherwise. Examining the developmental progress of low and high risk infants who had normal and abnormal newborn ABRs (i.e., I-V interval) in response to clicks, Murray found that newborn ABR was a low to moderately good predictor of delayed and impaired development during the first year of life. These discrepancies highlight the need for additional research in this area, and they also raise an important question about newborn ABR, namely, what exactly do we hope to predict using newborn ABR. Is our goal to predict, specifically, auditory system dysfunction or to identify infants at risk for more diffuse CNS dysfunction?

Since the goal of early identification of at risk infants is early intervention, and interventions for auditory or language dysfunction would be more circumscribed than those for general developmental delay (which may encompass a variety of other domains, e.g., motor functioning), some clarification of this point is needed by investigators in the field. Indeed, perhaps these "discrepancies" across studies regarding the success of ABR in predicting developmental outcome reflect the fact that researchers are trying to utilize ABR to predict somewhat different things. Eggermont is concerned with using ABR to predict permanent hearing loss. By contrast, Murray's interest is in using the same measures to identify infants at risk for general CNS dysfunctioning, which may or may not include auditory or language problems. The fact that the latter meets with greater success than the former suggests that newborn ABR may prove most useful as a screening device for general developmental delay or impairment. Extending its utility to identify children at risk for hearing or language problems *per se* will likely require the inclusion of additional measures that specifically tap these domains.

There have been a few attempts to correlate ABR and behavioral audiometry in predicting hearing outcome from infancy. However, this is an area in which additional research is sorely needed.

B.A.M.

In his review of the development of sensory activity in the auditory system, Eggermont focuses on the contribution of auditory evoked potentials. This excellent and thought provoking review discusses the evoked potential evidence for the onset of sensory activity in the auditory system and charts its maturation aspects. As well, Eggermont addresses two important clinical questions. What are the effects of auditory deprivation on the course of further development of the sensory system? And, what is the relationship between neonatal evoked potential screenings and the prediction of permanent hearing loss? My comments on Eggermont's review focuses on three points: First, what might be, in the broader context of auditory processing, the significance of the maturation observed for evoked potentials? In this discussion I will refer to a small portion of the extensive literature on infant speech perception, emphasizing research relevant to estimation of the

onset of auditory processing for speech perception. Secondly, what is the evidence from related areas on the effects of auditory sensory deprivation? For this discussion I will highlight research findings in both children and adults describing the effects of deprivation. Thirdly, I will briefly discuss several issues related to the efficacy of neonatal screenings.

Eimas, Siqueland, Jusczyk, and Vigorito (1971) initiated the field of infant speech perception by demonstrating that infants as young as about 44 weeks conceptual age (CA) could discriminate the voicing contrast in two synthetic syllables. This extraordinary observation showed clearly that the infant auditory system, even at this early age, is well-formed and provides a sufficient coding of speech sounds to support discrimination. Yet, at this same point in auditory development, almost all auditory evoked potentials are still undergoing maturation (except for wave I in the ABR). The maturation time of several years for auditory evoked potentials contrasts sharply to infant speech perception abilities near birth. It appears that adult-like auditory evoked potentials are not necessary to perform adult-like speech discriminations. Eilers et al. (1977) showed that speech sound discrimination continues to improve with age. This improvement parallels the reduction in latency of various components in AEPs and likely reflects an improvement in the coding of timing information as well as the continued emergence of a centrally based language function. Kuhl and Meltzoff (1982) showed that infants as young as 57 weeks CA can recognize which of two competing visually presented signals accompanies the speech sound heard (akin to speech reading). DeCasper and Fifer (1980) showed that 3-day old infants could identify the voice of their mother (speaker identification). These findings indicate that the sensory input, by the age of 57 weeks CA, is of sufficient quality to support an amazing array of auditory behaviors, well before complete maturation of auditory evoked potentials. Even though infant auditory evoked potentials show significant changes in response latency with increases in CA, the significance of these changes remains to be shown. Do these latency reductions mark a significant milestone in the overall development of the child?

Eggermont questions the effects of auditory deprivation in early life on further auditory development. One aspect of this question, which immediately comes to mind, is the concern often expressed by many clinicians and researchers about the effects of otitis media on language development. Friel-Patti, Finitzo-Hieber, Conti, and Brown (1982) followed a group of 35 at risk infants over the first 24 months of life. Fourteen of the infants were either free from otitis media or experienced only one episode during this period. These infants had a language delay incidence of 21%. In contrast, infants in the otitis media prone group (3 episodes or more) had a 72% incidence of language delay. In a prospective study of the effects of otitis media Feagans,Sanyal, Henderson, Collier, and Appelbaum (1987) suggest that three or more otitis media episodes can lead to a higher order language dysfunction. Feagans et al. believe that poor attention skills, resulting from multiple otitis media experiences, account for many of the long-term developmental problems. In addition to these lines of research, many retrospective studies have suggested that significant language delays result from otitis media (see Berko-Gleason [1983] for a brief review). More germane to Eggermont's question, are the reports by Folsom, Weber, and Thompson (1983) and Lenhardt, Shaia, and Abedi (1985) that childhood recurrent otitis media can result in prolongation of wave III. However, these reports differ as to the effects of otitis media on wave V latency. The reader should be cautioned that retrospective childhood studies must be interpreted carefully as there often are many non-controlled factors that could account for the language or AEP deficits observed.

An adult study pertinent to this deprivation issue was conducted by Silman, Gelfand, and Silverman (1984). Adults, fitted with monaural hearing aids, showed significant reductions in speech recognition scores in the unaided ear over a 4-5 year period, while hearing sensitivity remained unchanged. Again this is a retrospective study; longitudinal well controlled investigations are needed to provide insights into the possible mechanisms and confirmation of the findings. However, the study has implications for Eggermont's comment that the auditory system remains plastic well into adulthood. Our auditory system might well require a relatively never-ending sensory input to remain functional for speech processing, thus demonstrating a unique form of plasticity. In addition to a possible "critical period," there may also be a "use it or lose it" rule.

As a final comment on the deprivation issue, I would like to briefly mention my thoughts on Eggermont's suggestion that the MLR and SVP evoked potentials can be used as a measure of developmental abnormalities. As intuitive as this suggestion is, I would like to remind the reader of the report by Hecox and Hogan (1982) indicating that each of these two responses were present in approximately 80% of their 50 language impaired children. In fact, the most frequently observed pattern was normal for ABR, MLR, and SVP. But, most children showed at least one of the three evoked potential responses as abnormal. Cone-Wesson, Kurtzberg, and Vaughan (1987) report a similar diffuse pattern of AEP abnormalities. Faced with such possible evoked potential outcomes we must interpret results cautiously; the presence of MLR and SVP responses does not prove normality of langauge function. Abnormality of only the ABR response may indicate more than peripheral dysfunction in children at risk for language deficits.

Eggermont broadly outlines a follow-up hearing assessment program as an extension to current ABR screening

programs. The purpose of his follow-up program is to improve the ability of the combined programs to detect permanent hearing loss. Such additional steps are necessary due to the significant reduction in accuracy for estimating hearing sensitivity with only a click ABR predictor. Murray, Javel, and Watson (1985) surveyed published data from a variety of studies and found that approximately 13% of the 4,945 high-risk neonates screened have been followed later. Their compilation provides a screening follow-up population of 658 infants, 48% of whom had passed an initial screening. Given this overall follow-up rate, we lack the necessary data to refine ABR screening protocols using objective methods. Close scrutiny of their database reveals a disturbing statistic for infant follow-up rates. My concern is with the estimate of follow-up rate for high-risk infants failing initial screening. First, I excluded from the calculations data from those studies that attempted to follow all infants screened. I feel these studies are highly atypical of clinical service programs and reflect the efforts of well designed and staffed research programs. With the remaining data I calculated the ratio of the number of infants followed divided by the number of infants failing an initial screening. On an individual study basis, 65% or fewer of the high-risk infants failing initial screening are followed-up in later evaluations. This follow-up rate is appalling given that one goal of ABR screening is to identify infants for further evaluation to rule out the presence of significant permanent hearing loss. Hopefully, this low follow-up rate reflected a lag between initiating a screening program and putting into place follow-up procedures. If this is the case, then a survey of 1989 follow-up rates in high-risk infants failing ABR screenings might show a significant increase. On the other hand, things may not have changed; health resources are limited, and therefore the challenge of increasing the sensitivity of ABR screening procedures to detect permanent hearing loss in neonates will be most pressing.

The recommendations of the Committee on Hearing, Bioacoustics and Biomechanics, Working Group on Brainstem Audiometry of Prelanguage Groups (1987) can help to standardize neonatal screening programs. Unfortunately, the working group's report did not incorporate recommendations to increase the effectiveness of the ABR as a measure of hearing sensitivity. We cannot change the inherent sensitivity of the ABR measure. But, we can maximize the effectiveness of this measure by utilizing methodologies of the type suggested by Eggermont. In addition to the methods cited by Eggermont, the reader should follow the development of a technique recently described by Gorga, Kaminiski, Beauchaine, and Jesteadt (1988). They showed that spectral shaping of tonal stimuli, using cosine squared rise/fall times, to be promising in eliciting responses from specific frequency regions along basilar membrane. Validation of their method is needed with both hearing impaired and infant populations. Clearly, frequency specific ABR measures are possible and will continue to be refined. The optimal methodology needed to achieve acceptable accuracy in the prediction of hearing sensitivity as well as evaluation of the feasibility of the methodology in settings where neonatal screening are typically conducted remains to be undertaken.

J.C.B.

Eggermont presents an excellent review of research on the onset and development of auditory function and provides clinicians with a theoretical framework for the interpretation and understanding of ABR's. In my commentary, I would like to expand on some of Eggermont's statements with regard to the clinical application of ABR as a test of auditory function for graduates of the NICU.

Middle Ear Effusion in Infants

Eggermont discusses the high incidence of middle ear effusions in newborns of the NICU, making it difficult to identify truly significant hearing losses. This problem is very real, and a cost effective neonatal screening program must make sure not to retest many infants whose hearing loss may be transient. In a study of 600 graduates of a NICU tested with ABR (Durieux-Smith, Picton, Edwards, MacMaurray & Goodman, 1986), we found that the incidence of failure (no response at 30 dBnHL in one or both ears) decreased by 10% if the babies were initially tested post discharge at 3-5 months corrected age (age since birth less degree of prematurity). A high proportion of the babies who had just failed the test (response at 40 dBnHL but not at 30 dBnHL) when tested prior to discharge in the NICU, passed when retested at follow-up. These babies were younger at initial test than the ones tested at 3-5 months corrected age. Many of them had mild transient hearing losses that resolved spontaneously. Failures that give rise to normal results at follow-up have been called false positives of the ABR method (Cox, Hack, & Metz, 1984; Roberts, Davis, Phon, Reichart, Sturtevant, & Marshall, 1982; Simmons, 1983). It is more likely, however, that ABR did correctly identify a dysfunction present at time of test. A cost effective approach to ABR testing of NICU graduates may be to test the babies post discharge at 3 months corrected age.

Target Population

Another problem with the use of ABR to screen NICU graduates is the definition of the target population to be identified. The definition of what constitutes a significant hearing loss has varied from study to study. It has been described as a permanent disorder that might benefit from early clinical management (Murray, Javel, & Watson, 1985) or as a condition requiring otological care or audiological educational management (Stein, Ozdamar, Kraus, et al., 1983). A comprehensive program should probably address any hearing loss

which may affect communicative development (Rapin, 1978, Ruben, Umano, & Silver, 1984). Children with cleft palate and Down syndrome may have long standing conductive losses that will affect speech and language development and should also be identified early in infancy.

Prognostic Validity of ABR

A final point has to do with the prognostic validity of ABR. The basic question is whether ABR can enable us to identify children with impaired hearing requiring management and those with normal hearing. Many studies of ABR in high risk infants do not report follow-up or the proportion followed is very low (Murray et al, 1985). In some studies, only babies with abnormal ABR results are followed (Murray et al, 1985). What is of interest to the clinician is the relationship between ABR and the pure tone audiogram.

We have obtained audiograms on 333, three year old children who were graduates of a NICU and tested in infancy with ABR using clicks (Durieux-Smith et al., 1988). Our results are encouraging. Of 294 children who were identified as normal with ABR, 277 (94%) had normal audiograms bilaterally. Twelve (4%) children had conductive hearing losses with conventional audiometry; these could have developed subsequent to ABR testing. Five children had a sensorineural loss that had not been identified with BERA screening. Four of these (3 unilateral, 1 bilateral) had an unusual configuration with thresholds of 35 dBn HL or better in the 1000-4000 Hz frequency range. One child had a flat unilateral sensorineural loss that could have developed subsequent to ABR screening.

ABR is a powerful tool in the evaluation of auditory function in infants, but audiologists must be aware of its limitations. ABR using clicks is not a predictor of audiometric contour and corresponds to hearing sensitivity in the 2000-4000 Hz area. Some children with sensorineural losses of unusual configuration with normal sensitivity around 2-4 kHz may not be identified with ABR. Frequency specific ABR may be important if adequate normative data is available and if rapid testing protocols can be used. ABR using bone conduction also is helpful for differential diagnosis. Hearing losses can develop subsequent to ABR testing, and a normal ABR result is not a guarantee of normal hearing in later life. An abnormal ABR result in an infant signals a need for audiological follow-up.

A.D-S.

Eggermont has provided us with a very comprehensive review of studies concerning changes in evoked potentials during the development of the auditory system. There are two separate areas on which I would like to comment and invite Eggermont's point of view. The first concerns the onset of auditory function in humans and the much asked question of how much a fetus actually hears in utero. Should concerned parents talk to their child before its birth, and play Brahms and Beethoven (to prevent "heavy metal" addiction later in life)? When asked such questions, I usually draw attention to the impedance mis-match between airborne sounds and the water of the body and uterus, resulting in relatively little transmission of the vibrations in the air to the body. Eggermont's article mentions two further attenuating factors, that of the insulation due to the maternal abdominal and uterine walls themselves and the existence of a relatively high background noise in the uterus. It would seem that other than mother's vocalizations or extremely high intensity environmental sounds, there is very little transmission of acoustic information to the fetus. I would be very interested in hearing Eggermont's viewpoint on this somewhat controversial subject.

My second comment is more academic in nature. The use of evoked potentials is one of the very few "windows" through which we can monitor the development of auditory function. I would like to make a cautionary note to stress that the window is rather small. The evoked potentials themselves represent a small subset of electrical events occurring in the auditory pathways as a result of sound stimulation. In brief, they represent those neuronal pathways which provide a synchrony of unit events sufficient to yield a recordable potential at some considerable distance from their point of origin. With regard to brainstem evoked potentials, it is most likely that the standard ABR recordings are reflecting one particular pathway, namely that from the AVCN through the superior olivary complex and then to IC. The ABR will give very little information, perhaps none, concerning activity in the dorsal cochlear nucleus and its afferents to IC.

I use this as an example to indicate that the "take home" message from the evoked potential studies with regard to the maturation of the auditory system applies only to those parts of the auditory system that are being monitored with this technique. Thus an apparent maturation of brainstem evoked potentials does not necessarily mean that all auditory areas in the brainstem are, in fact, mature. There may be reason to suppose, for example, that the dorsal cochlear nucleus has a much longer period of maturation than AVCN. The same principle applies to other levels of the auditory system.

Eggermont has a very elegant "simple model for developmental changes" in which he considered the maturation of auditory system structures mainly relating to myelination and synaptic changes. Taking a more holistic view of the system, I would invite comments on the possibility that the descending pathways and their maturational processes will have some influence on what activity is allowed to ascend in the system. I am not being critical of Eggermont's model for describing

developmental changes, he makes it quite clear that this is only a first approximation. However, I do invite his comment on some of the other possible factors which could be influencing the latency changes observed.

Finally I would like to be provocative, again to provoke comment, and state that in all probability the higher levels of the auditory system are never fully mature. It is clear, mainly from studies in the somatosensory system (e.g., Merzenich & Kaas 1982), that the primary cortical areas can be dynamically altered with changing experience and is thus are never developed to an end-point. This may also be true of subcortical regions, and of course it is absolutely the situation with secondary cortical areas and beyond. Again then, I am making a cautionary note to the effect that the stabilization of evoked potential waveforms and their latencies is not necessarily a reflection of the maturity of the whole auditory system. This, if we use evoked potential data to define a particular developmental epoch, we should do with extreme caution and recognition of the limitations of the viewing technique.

R.H.

Eggermont's review of the auditory development literature makes the strong suggestion that the limiting factor in the so-called "onset of hearing" in mammals is the maturation of the cochlea, since neural responses can be recorded as soon as, or very shortly after, cochlear responses. Certainly this conclusion is supported by the studies Eggermont cites. However, one must be careful not to overinterpret this result. Although responses can be recorded from the central nervous system with the first cochlear response, that does not imply that the central nervous system is mature at this time, even in its most basic response properties. While cochlear development does seem to drive the development of absolute sensitivity (e.g., Aitkin & Moore, 1975; Brugge, Javel, & Kitzes, 1978; Brugge, Orman, Coleman, Chan, & Phillips, 1985), Sanes and Rubel (1988) have recently presented evidence that maturation central to the cochlea contributes to the development of frequency resolution in the gerbil auditory nervous system. Moreover, there are several lines of evidence which suggest that the time course of development of temporal coding in the auditory system is prolonged beyond the period of cochlear development (e.g., Brugge et al., 1978; Sanes & Constantine-Paton, 1985). Thus, the auditory system is not simply becoming more efficient after the cochlea begins to respond; some of the most basic stimulus coding properties of auditory neurons continue to develop as well.

The observation that temporal coding takes some time to mature may in fact be related to Eggermont's own observations with respect to the development of ABR latency in human infants. Although increased myelination and synaptic efficiency would have the effects on ABR latency that Eggermont suggests, it is also the case that in order to record the ABR, a synchronous discharge of auditory neurons must take place. This is the reason that the ABR arises primarily from the basal region of the cochlea, where traveling wave velocity is high. It also accounts for the failure to measure ABRs in individuals suffering from multiple sclerosis, as r. Eggermont notes. If the immature auditory system is unable to produce such precisely timed discharges, then it is likely that this will influence the characteristics of the ABR measured from that system.

The dependence of the ABR on synchronous neural events is both a strength and weakness of the approach for the study of development. The strength is that the ABR may provide a method for following the development of temporal coding in human infants. At the same time, it is clear that the ABR cannot be taken as an unambiguous indicator of the functional status of the auditory system during normal development, for changes in temporal coding may have little impact, say, on absolute sensitivity. The extent to which age-related changes in the ABR reflect functional maturation of hearing has yet to be established.

A final important point is that the infant ABR may not be as well correlated with high-frequency sensitivity as the adult ABR is. For example, Folsom and Wynne (1986, 1987) have recently shown that lower frequencies (1000 Hz) make a greater contribution than higher frequencies (4000 Hz and higher) to the infant ABR than they do to the adult response. This effect was observed as late as 3 months postnatal age. That is not to say that the ABR is generated more apically in the infant's cochlea; this finding may be related to the changes in tonotopic organization reported by Rubel and his colleagues, cited by Eggermont. However, the point should be made that interpretation of the infant ABR may not be as straightforward as we once thought.

L.W.O.

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Eggermont's Reply to Commentaries

The points raised by the commentators can be combined into five separate questions:

1. Is there any chance that airborne environmental sounds such as classical or rock music are effective in shaping the fetus' future outlook on life? (Harrison)

2. What, if any, is the role of the descending efferent system on the maturation of the auditory system and the way this is reflected in evoked potential latencies? (Harrison)

3. Is the auditory system permanently plastic, and therefore is continued stimulation required for optimal performance? (Harrison, Booth)

4. Are evoked potentials at all relevant in the understanding of auditory maturation? (Harrison, Booth, Olsho)

5. What is the efficacy and prognostic value of ABR testing in NICU? (Durieux-Smith, Booth, Morrongiello)

I want to stress that answering these questions is not an easy task. The questions relate to the very essence of the paper and demonstrate how little ground my paper has covered and how formidable the size of the problem still is.

Is there any chance that airborne environmental sounds such as classical or rock music are effective in shaping the fetus' future outlook on life?

Four factors determine whether airborne environmental sounds can stimulate the fetus: (1) the attenuation from air through maternal tissue and the fluids surrounding the fetus; (2) the intrauterine noise spectrum; (3) the level and spectral content of the environmental sound (e.g., music); and (4) the middle ear function in the fetus.

Let me remark that there will be a rather efficient transmission of sounds produced by the mother (heartbeat, voiced speech) since the attenuation factor for such, internally transmitted, sounds is virtually absent. The attenuation spectrum (Walker et al., 1971) for the maternal tissues and the air-fluid mismatch is about 30 dB at 50 Hz, 35 dB at 200 Hz, 40 dB at 1000 Hz, 50 dB at 2000 Hz, 75 dB at 4000 Hz, and more than 90 dB for higher frequencies. Thus at low frequencies we only have the mismatch factor of 30 dB, supplemented for higher frequencies with the increasing tissue attenuation.

The background noise in the uterus (Walker et al., 1971) is about 80 dB SPL at 20 Hz, 70 dB at 50 Hz, 60 dB at 100 Hz, and 50 dB at 200 Hz, decreasing to less than 40 dB SPL at 500 Hz. Thus it consists of mostly low frequency noise with a mean overall level of 85 dB SPL and with a peak maternal heartbeat pulse of 95 dB SPL. Combination of the attenuation and the amount of masking shows that the most sensitive region is around 1000 Hz (the speech range) with about 40 dB attenuation. Rubel (1978) estimates the overall noise level to be higher and amount to about 75 dB SPL in the 200-800 Hz range.

The most important factor is the middle ear function of the fetus with its fluid filled middle ear. Since sound in the uterus is transmitted by fluid, the coupling to the middle ear will be quite efficient. Because nothing is known about the overall efficacy of transmission, any further discussion is pointless. We cannot estimate what the fetus is actually hearing. We can, however, estimate to what sounds a fetus is reacting (see my paper and Granier-Deferre, Lecanuet, Cohen, & Busnel, 1985); such sounds always have an intensity over 105 dB SPL. Classical music usually does not have this intensity in the range of speech frequencies that are most readily transmitted, hard-rock often does. So if anything will cause fetal reactions, rock music played at disco sound level is a likely candidate. How this shapes the future music appreciation of the fetus remains an open question.

What, if any, is the role of the descending efferent system on the maturation of the auditory system and the way this is reflected in evoked potential latencies?

We only recently started to appreciate the effects of the efferent system on various auditory processes (Liberman, 1988). However, no study is known to me that describes the maturation of the neural activity in, say, the olivo-cochlear bundle. Walsh and McGee (1988) suggest, on basis of combined electrophysiological and pharmacological studies, that early in the development of the cat (less than 2 weeks old) there is a specific effect of the olivo-cochlear bundle upon the inner hair cell output. The comparable period in humans is somewhere at the beginning of the third trimester. What we know (Figure 8 in the paper) is that the efferent innervation of the outer hair cells in humans starts at about 5 months CA and is completed at 7 months CA. We expect that the myelinated crossed olivo-cochlear bundle (COCB) will undergo the same changes as the afferent nerve tracts, such that the speed of transmitting the efferent action potentials will increase over the first 3 years of life. The unmyelinated uncrossed OCB will not undergo that maturation and may exert its full potential from whenever the synapses in the cochlea are formed. A more effective efferent system will increase response threshold and increase response latency under certain, especially binaural, stimulus conditions. The potential interaction between the maturing afferent system and the gradually more effective descending system, a type of feedback problem, is hard to predict and entirely speculative (for some speculation and mathematical modelling see Eggermont, 1985).

Is the auditory system permanently plastic, and therefore is continued stimulation required for optimal performance?

One of the most dramatic demonstrations of adult brain plasticity was reported by Merzenich and coworkers. They demonstrated that receptive fields in the adult monkey somatosensory cortex are alterable by lesions in the sensory periphery, such as median nerve section or digit amputation or by increasing peripheral stimulation (Merzenich & Jenkins, 1983). There are two types of mechanisms that can explain this central nervous system plasticity in adults. The first is that previously ineffective connections become effective in activating cortical neurons as a result of local changes in the amount of inhibition or an increase in sensitivity. Secondly, new connections may be formed through axon growth and/or dendritic extension. While the tonotopic organization in auditory cortex is the result of hard-wired connections and largely indicated by the organization of the anatomical projections, sound localization which is represented across isofrequency domains must be organized by experience and will be alterable throughout life (Merzenich, Jenkins, & Middlebrooks, 1984). Such alterations probably involve changes in the strength of pre-existing synapses. Variability in brain structure also is found in organisms that have the same genetic make-up, illustrating that environmental factors and individual differences are important for shaping the brain (Changeux & Danchin, 1976).

It has been clearly established that the dorsal auditory pathway, projecting from the dorsal cochlear nucleus to the surround nuclei of the inferior colliculus and to the magnocellular part of the medial geniculate body, does show learning related changes. This non-lemniscal tract projects to the magnocellular part of the MGB (MGm), which is not topographically organized and equipped with units that have very broad tuning curves. Neurons in the MGm are not very selective for differences in physical sound parameters, but develop plasticity during learning (Weinberger, Hopkins, & Diamond, 1984). The primary auditory cortex (AI) receives input from the non-plastic part of the medial geniculate nucleus onto the middle layers, and from the plastic MGm onto the upper layers. Only part of the cells in AI appear to be plastic. The secondary auditory cortex (AII) receives its input directly from MGm and indirectly from MGv through AI; all cells in AII develop plastic response properties.

These physiological facts combined with the anecdotal but still highly suggestive findings in adults fitted unilaterally with hearing aids suggest that any imbalance of stimulation through the two ears will have an effect on the strength of the synaptic contacts in the primary auditory cortex. This will among others create a new spatial map of the auditory world that may well differ from that for two identical ears.

Are evoked potentials at all relevant in the understanding of auditory maturation?

To discuss this topic requires a somewhat detailed overview of the auditory nervous system and a reflection upon what subgroup of neurons is likely to contribute to evoked potentials in general. Evans (1975) has suggested a ventral and a dorsal division of the auditory pathways, the separation of which occurs as peripheral as the cochlear nucleus complex. The ventral pathway starts at the ventral cochlear nucleus, passes through the superior olivary complex and the lateral lemniscus in order to arrive at the inferior colliculus. The ventral pathway also is known as the lemniscal pathway. The dorsal pathway begins at the dorsal cochlear nucleus and proceeds via the dorsal acoustic striae directly into the inferior colliculus, hence it is called the extra-lemniscal pathway. The lemniscal pathway neurons have auditory nerve fiber like properties, sharp tuning and dominantly sustained responses to sound.The neurons in the dorsal pathway have, in general, more complex response properties.

Based on the neuronal properties one can extend the lemniscal system onto the ventral part of the medial geniculate body (MGv) and the primary auditory cortex (AI).The extra-lemniscal pathway proceeds via the dorsal and magnocellular parts of the MGB onto the non-tonotopically organized parts of the auditory cortex (among others the AII). Most units in the dorsal pathway have labile, not very reproducible responses, are broadly tuned, have long latencies, and are inaccurate responders. Evans (1975) suggested that the ventral pathway is involved in accurate localization and the dorsal pathway, in the identification of meaningful sounds.

The brain stem electric responses are in all probability produced by neurons in the ventral pathway, more specifically by neurons that fire in a strong time-locked fashion to click and tone-burst stimuli. Short latency evoked potential studies therefore will tell us most about localization, tuning, timing, and tonotopy in the auditory nervous system and not so much about meaning, perception, and cognition.

What about the cortically generated evoked potentials? The MLR and SVP as discussed in the paper are most likely generated in the AI and AII, respectively (Scherg & Von Cramon, 1986) and seem still to reflect mainly the lemniscal part of the auditory system, although they are influenced by attention. The so called event-related potentials with long latencies such as the P300 are influenced by meaning, since they are task related or respond to odd-ball stimuli and thus are related to some aspects of behavioral sound processing.

The parameters of the evoked potentials that have received most attention are latency measures, basically because there is an orderly progression of latency with age. Latency and synchronization of neural activity are effected by

various subject related variables, the most important of which are degree of myelination and efficacy of synapses. An important stimulus variable is the rate of rise of the stimulus. ABRs are only evoked by stimuli with rapid onset such as clicks and tone-pips. Synchronization of the activity of nerve cells therefore is a prerequisite for the recording of an ABR. This requirement is progressively relaxed towards the more cortical responses, but a stimulus change is still required. As the potentials acquire longer latencies and are generated more in central cortical areas, meaning and newness have an effect on amplitude but usually not on latency. We are only starting to appreciate the behavioral factors that can influence the various event-related potentials.

Evoked potentials are windows to the brain, windows equipped with intricately wrought louvre shutters, that allow us glimpses of what is happening inside. In our recordings we only see shades that may or may not fit with the ideas we have in mind when we do our testing. The shades on their own are little more than Rorschach tests for the electrophysiologist interested in the human brain. When we use ABRs in NICU, we know what we want to see and therefore can make excellent use of them. In order to correlate SVPs and event-related potentials to phonemic discrimination and voice recognition, we need a concrete hypothesis about what aspects of the evoked potentials are likely to reflect this. If we do not have such a hypothesis, devising a test is hopeless. Thus, evoked potentials will never be a substitute for hearing tests by behavioral means; they form however a very powerful complement.

What is the efficacy and prognostic value of ABR testing in NICU?

I can completely agree with the remarks made by Durieux-Smith and Booth regarding the practice and purpose of the ABR screening in NICU. The very fact of the large number of middle ear effusion cases makes it nearly impossible to predict the hearing status at, say, 1 year. However, ABR-testing can screen very effectively for more severe hearing losses and, in any doubtful case, can request follow up ABR within a few months. Persistent conductive hearing losses thus can be spotted: after all they may impair proper language acquisition just as much as sensorineural losses. If one were to ask the question "To ABR or not to ABR?" I can just repeat what I said under another title (Eggermont 1985b): "Audiometric ABR testing requires much more effort than click screening, however this (Audiometric ABR using tone-pips) is generally used at a critical stage in the development of the child where rehabilitation can no longer wait... How to balance the more extensive testing required against possible prevention of setbacks due to hearing impairment is a difficult but necessary component of a cost/benefit analysis." At present I believe that click-ABR is the minimum test that one can and has to perform in order to screen the residents of the NICU.

With respect to Morrongiello's comment that Murray's recent study found "ABR a low to moderately good predictor of delayed and impaired development during the first year of life," I can add that this is confirmed by our own findings. In a study in 224 VLBW infants (Eggermont et al., in preparation, some detail included in the main paper) we found that predictions of future values of I-V interval and V/I amplitude ratio on the basis of measurements in NICU were possible up to about 11/2 year. However, this only indicates that after this period there are no persistent abnormalities at the brainstem level, although there frequently are signs of retardation in development later on in these children. These signs also can be found in cases with normal ABR values in NICU. Thus it seems that the value of ABR to predict diffuse CNS dysfunctions is not as clear as the comment suggests. I doubt the usefulness of ABR as a screening test for general developmental delay. It has been suggested on the basis of the high incidence of abnormal ABR findings in mild to profound children with retardation (e.g., Mochizuki, Ohkubo, Yoshida, & Tatara, 1986) that the I-V delay may serve to further quantify retardation in development. However, Mochizuki et al. found a prolongation in the I-V interval in only 5% of cases and always accompanied by a neurological abnormality.

It must be stressed once more that ABR usually is used synonymously for click ABR. However, the click is only one of the many possible stimuli that can be used to evoke a brainstem potential. The correlation of ABR results obtained in NICU and behavioral audiometry later in life is expected to be as good as was found for electrocochleography (Spoor & Eggermont, 1976; Parving & Elberling, 1982) in cases in which frequency specific stimuli are used. Prediction on basis of click ABR has to be done with care. Durieux-Smith's last paragraph summarizes the situation very aptly and additional research is not going to change this. It is not a matter of research but a matter of choice as to what ABR method to use given limited resources and time to screen all NICU residents and to determine which ones to follow up later in life.

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