MY MASTER AND MY LIVING GOD

"Like a bundle of blessings he packs
himself
into every moment of my life"

AGE RELATED VARIATIONS IN P_{300} IN THE GERIATRICS

Reg.No.M9014

AN INDEPENDENT PROJECT WORK SUBMITTED IN PART FULFILMENT FOR FIRST YEAR M.Sc., (SPEECH AND HEARING) TO THE UNIVERSITY OF MYSORE.

ALL INDIA INSTITUTE OF SPEECH AND HEARING: MYSORE-570006

1991

C E R T I F I C A T E

This is to certify that this Independent Project entitled: **"Age related variations in P_{300} in the geriatrics"** is the bonafide work done in part fulfilment for first year M.Sc., (Speech and Hearing) of the student with Reg.No.M9014.

Mysore
1991

Director
All India Institute
of Speech & Hearing
Mysore-6

CERTIFICATE

This is to certify that this Independent Project entitled: **"Age related variations in P_{300} in the geriatrics"** has been prepared under my supervision and guidance.

Mysore
1991

Dr.(Miss) S.Nikam,
Prof, and Head,
Audiology Department.
GUIDE

DECLARATION

This Independent Project entitled: **"Age related variations in P_{300} in the geriatrics"** is the result of my own study, undertaken under the guidance of Dr.(Miss) S.Nikam, Prof, and Head of the Department of Audiology, and Director, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier at any University for any other diploma or degree.

Mysore

1991 Reg.No.M9014

ACKNOWLEDGEMENTS

At the outset I'd like to express my tender thanks to my guide Dr.(Miss) S.Nikam, Prof, and HOD, Dept. of Radiology, All India Institute of Speech and Hearing, Mysore, Mysore, who integrated this project into a meaningful whole.

My hearty acknowledgements to Dr.(Miss) S.Nikam, Director, AIISH, Mysore, for having given the permission to make use of the facilities to conduct this experiment.

Thank you subjects for so patiently volunteering.

None of this would have been possible without the patience of Mrs.C.S.Vanaja, Audiology Department, who found several subroutines when the 'disc' got struck in the rut. I & m very grateful to her.

Saya-Manna from heaven - the minstrel who not only helped me to find subjects,also pumped me with courage and determination during the low ebbs.

I thought, I would be unable to finish it ... when Pragna, Jyothi, Raghu, Nandu, Ships said,"C'mmon, Have the courage to live. Anyone can die".

Jeny's love sometimes shaken when the going is calm gathered strength during "The storm" "10Q Aparan".

Amma and Appa - It is very difficult to explain. But you understand and that makes all the difference. What would I have done without your assistance?

I am sure that this is a better work as a result of Mr.Venkatesh, keeping my nose to the grindstone. Like a supernova, you helped me in every stage of this work. I shall not use words. To define is to limit. Otherwise its unique, transcendental and infinite.

My other acknowledgement is on the dedication page of this project - my mentor. I KNOW THAT YOU KNOW.

Kudos to Mrs.Rajalakshmi for her deligent, destrous, and fantabulous typing.

TABLE OF CONTENTS

INTRODUCTION

"....Let us discuss some aspects contributing to a description of variables and facts important for the assessment of that which makes up the stage of ontogenesis which we refer to as "Elderly"

- F.Hoffmeister.

In an effort to enhance the objectivity in the assessment of central processing disorders, interest has focussed on the use of electrophysiological measures (Musiek and Baran, 1987).

Many of these investigators involved the Auditory Brain Stem Response (ABR) and its use in the evaluation of various retrocochlear lesions. While the ABR has been shown to be very sensitive to VIII nerve and lower brain stem (BS) lesions its usefulness in the assessment of upper BS and cortical lesions is limited (Musiek and Baran, 1987; Wada and Starr, 1983).

Consequently renewed interest have been shown in the later waveforms - the middle latency response (MLR) and long patency potentials (LLP) as possible ways of objectively delineating problems in the central auditory system.

While many investigations suggest that the MLR has potentially valuable clinical applications, its usefulness is hampered by the still unresolved issues surrounding origin, maturational effects, as well as the influence of technical parameters on the test outcomes (Fifer, and Sierra Irizarry, 1988; Jerger, Oliver, and Chintel, 1988; Musiek, Verkest and Gollegly, 1988).

Partially as a consequence of these limitations renewed interest has also focussed on potentials occuring after the MLR.

Like the MLR, LLP have been investigated for a number of years. These later responses tend to be more variable and consists of both stimulus exogenous potentials (SRP) and Event related potential (ERP) (Polich and Starr, 1983). The SRP consists primarily of a negative peak N_1 occuring at about 80-100 m.sec., a postive peak P_2 occuring at approximately 140-220 m.sec. and a small negative peak, N_2 at about 280-320 m.sec. (Kileny, 1982; Mason and Mellor, 1984).

The ERP which are elicited by internal cognitive activities through various sensori modalities, consist of a variety of highly variable waveforms occuring beyond N_2 (Kileney, 1985; Musiek et al. 1988) of these responses,

the most studied has been the P_{300} component occuring roughly from 300 - 700 m.sec. (Hall, 1989? Kilney, 1985? Mason and Mellor, 1984; Musiek et al. 1988; Squires and Hecox, 1983). Picton, et al. (1977) stated that "They are the best evoked potentials measurements available, if they can be reproduceably recorded "as their presence indicates the complete integrity of the auditory pathway in the central nervous system (CNS).

While the origin of the SRP is cortical with probable generator sites in the auditory cortex of the superior temporal lobe, parietal and frontal association areas(Picton et al. 1974? Mason and Mellor, 1984) the P_{300} ERP originate from nonspecific unknown neural generators and is felt to be an electrophysiological manifestation of strategies used by CNS in selective attention activities, including frontal cortex (Courchesne, 1978) centre parietal cortex (Simson, et al. 1977) and auditory cortex of superior temporal lobe (Kilney, 1985), Hippocampus and associated brainsites (Okada, et al. 1983).

Eventhough the decade of 1960 was predominant with findings in long latency response (LLR) (Davis, 1964) 1970s was dominant with ABR. But there is a renewed interest in late potentials and of special importance is the P_{300}.

After about 250 msec, the general characteristics of auditory evoked potentials (AEP) change from those of uniform response to highly variable and subject dependent manifestations of perceptual and cognitive activity.

P_{300} is an event related potential require the subject to be actively engaged in a task usually an information processing task. The P_{300} component can be obtained with a number of stimulus presentations (auditory, visual or somatosensory stimuli) (Donchin, 1979; Sutton, 1979; Snyder, et al. 1980) in which the subject processes task relevant information. The P_{300} component of ERP is considered to reflect aspect of cognitive processing. Its latency is thought to reflect the time taken to evaluate stimuli according to a number of factors including salience (Pritchard, 1981).

P_{300} is theorized to be relatively independent of evoking stimulus (Polich and Starr, 1981; Picton and Fitzgerald, 1983; Weinberg, et al. 1984). The response occurs when an individual relates the incoming sensory information to memory updating processes (Donchin, 1981) and is considered to be unaffected by exogenous influences (Kilney and Kripal, 1987; Songberg, and Decker, 1990).

P_{300} component of the ERP is a large positive going waveform elicited whenever subject discriminates stimuli occuring approximately 300 m.sec. after the stimuli (Sutton, et al. 1967).

The most common situation for auditory stimuli is the oddball paradigm and consists af the subject counting rare occurrences of a target tone embedded in a series of more frequently occuring standard tones (low probability target (T) stimuli presented against a background of higher probability non-target (NT) stimuli) (Polich, 1986b).

CURRENT APPLICATIONS:

The late components are not used routinely in clinical hearing assessment. However the use of the P_{300} component to examine various clinical populations is a relatively new endeavour. Visual stimuli are employed to investigate forms of psychopathology (Roth et al. 1979), attention or memory abilities in the aged (Smith et al. 1980) as well as a variety of problems in human information processing (Donchin, 1979).

A number of studies have considered P_3 latency and amplitude as useful measures of assessing the cognitive function in both normals and neurophysiological disordered patients as P3 responses is directly related to the neuropsychological state of the individual (Musiek, et al. 1988).

The presence or absence of P_{300} using auditory stimulation is mediated through a central processing system consequently the absence/dealy of the P_{300} to auditory stimulation

may be the exclusive result of a problem in the central processing system Involved in coordinating all incoming sensori information.

P_{300} Potential has been used as an objective electrophysiological test to detect cognitive dysfunction occuring in dementia (Goodin, Squires and Starr, 1978a).

P_{300} latency increase also reflects the degree of cognitive decline in dementing illnesses (Polich, Enhler, Otis, Mandell and Bloom, 1986) and mental retardation (Squires, et al. 1980).

Effects of alcoholism, on P_{300} latency are well studied as confusional states (Polich, 1984).

P_{300} has been used to differentiate cognitive disorders such as depression from the Alzeihmer's type ie organic vs functional type. In children longer P_{300} latency has been liked to hyperactivity, schizophrenia, autism and reading disability with a few changes in P_{300} latency (Finley, Faux, Hutcheson and Amstutz, 1985).

NEED FOR THE STUDY:

However in order to use the late component of the ERP as a clinical tool. The alterations due to "normal" aging

must be well established. This is especially important . for the study of cognitive impairment, as the major alteration seen in dementia -prolongation of P_{300} latency -is also seen, but to a lesser degree in normal aging (Goodin et al. 1978b).

There is an essential need to collect normative data across age groups to adequately assess the age latency relationship of P_{300}.

The growing body of literature on the changes in ERP with age and the reports of success in applying the latency of P_{300} for the diagnosis of dementia prompted the research reported in this project.

The increase in P_{300} latency with age and the further increase with dementing illness suggest the attractive hypothesis that P_{300} is sensitive to age related cognitive slowing as well as to desease induced cognitive impairment (Pfferbaum, Ford, Roth, Kopell, 1984).

The current study was undertaken to test the following objectives.

1. There is age related significant variation in the latency of P_{300} on comparing geriatrics (50-70 years) and adults (18-22 years).

2. There is age related significant variation in amplitude of P_{300} on comparing geriatrics (50-70years) and adults (18-22 years).
3. There is age related significant variations in geriatrics of 50-60 years age and 60-70 years ages for P_{300} latency.
4. To determine the most accurate description of the relation between P_{300} latency and age among normals and geriatrics (ie to regress the subjects on their age and find if linear or curvilinear equation can be used to predict normal latency at a given age.

REVIEW OF LITERATURE

There is general agreement that the physical parameters of the eliciting stimulus, have a profound influence on the human average evoked potential waveform, particularly on components occnring within 250 msec, of stimulus presentation (Regan, 1972).

Researchers investigating perceptual/cognitive correlates of the AEP must always be careful not to attribute changes in the AEP waveform to changes when concomittant alterations of the physical parameters of the stimuli were also taking place.

Beginning with a report by Sutton, Braren, Zubin and John (1965), it has been demonstrated that a component of the human AEP existed that did not reflect the physical parameters of the eliciting stimuli. Rather this components appears to reflect active cognitive processing of stimulus information on the part of the subject.

This same brain component is elicited in certain experimental contexts regardless of the sensori modality of stimulus presentation (squires, Duncan-Johnson, Squires and Donchin, 1977).

The most common designation given to the component is P_{300}, referring to its polarity (positive) and approximate latency (about 300 m.sec) following stimulus presentation.

Other designations include P_{300} referring to the 3rd prominent positive component following stimulus presentation or otherwise called late positive component (Price and Smith, 1974).

Whether a given stimulus serves as a task relevant signal/non-signal is a function of the instructions given to the subject not of something intrinsic to the stimulus itself.

Since the same stimulus may/may not result in P_3 depending on the experimental context. It is more accurate to speak of P_{300} as being 'Invoked' by the stimulus than as 'Evoked'. Hence the term ERP is beginning to replace evoked potential in the literature.

NEURO ANATOMICAL AND PHYSIOLOGICAL ORIGINS OF P_{300}:

P_{300} latency has been found to decrease with increase in cognitive development stemming from maturation in children (Courc/esne, 1984? Howard, and Polich, 1985).

Adult aging (Goodin and Squires, 1978? Brown, Marsh, Larue, 1983; Polich, Howard, Starr, 1983) and neurological

impairment (Pfefferbaum, et al 1980; Lai et al. 1983; Eich Ehlers, Otis, Mandell, 1986) have been correlated with increases in P_{300} latency. In addition P_{300} amplitude variations have been associated with individual differences in memory function (Polich, et al. 1983? Davis, Donchin, Fabiani, 1984), differential inheritability of alcoholism (Neville, et al. 1982; Begleister, et al. 1984?; Polich, 1986) and the residual effects of alcohol consumption. Thus the P_{300} BRP component is beginning to provide an electrophysiological index of the cognitive processes that covary with physiological changes.

Endogenous electrical potentials appear at the scalp when a subject is engaged in tasks requiring judgements about the properties of a stimulus. Typically the components of task related potentials appear between about 200 and 600 m.sec. after the onset of the stimulus. The strengths of these components depend mainly on the relevance of the stimulus to the task and less on the sensory modality being stimulated or on the particular sensory property of the stimulus (Sutton, et al. 1965).

Thus these components are believed to reflect non-sensory, cognitive processes carried out by the human brain (Donchin, et al. 1978).

Intracranial recordings from epileptic patients revealed large extracellular potential gradients and increased single unit firing in or near the hippocampal formation and amygdala while the patients were performing tasks that elicited the endogenous potentials at the scalp (Halgren, et al. 1980; Wood, et al. 1980, 1983).

Magnetic fields detected with a SQUID senaor at the temporal and occipital areas of the head in response to a frequent and infrequent visual stimulus revealed sources of P_{300} lay deep in the brain within hippocampal formation and amygdalaid structures (Okada, Kaufman and Williamson, 1982).

Marked P_{300} waveform similarity have been found in monozygotic twins (Buchbaum, 1974).

Comparision of monozygotic and dizygotic twins have suggested a strong genetic basis for this similarity (Polich and Barns, 1987).

The morphological similarity in the twin waveform compared to the control pairs ERP suggests that the individual differences in the P_{300} component are determined by the underlying neurophysiological structures associated with its generation (Polich and Burns, 1987).

Thus P--n or P_3 component of the ERP is a large (10-20 /u0v), positive going wave form elicited whenever the subjects

discriminate stimuli. Possibly originating in the hippocampus and amygdaloid structures its production has been linked to the psychological processes underlying memory updating when the neural representation of the stimulus Environment is modified to accommodate incoming sensori-information (Donchin, 1981).

ELICITING P_{300}:

The most common situation for auditory stimuli is the "oddball" paradigm and consists of the subject counting rare occurrences of a target tone embedded in a series of more frequently occuring standard tones.

While the target tone is physically different from the standard tones, it is not the physical difference which produces the large positive going component bat rather the information supplied to the subject with the occurence of the relevent target tones (Sutton, et al. 1965? 1967). This is shown by the fact that the same response also is obtained by omitting a stimulus in a series of tones and having the subjects count the number of omissions (Picton et al. 1973.

P_{300} can be obtained with as few as 20-30 replications of target event.

The same can be elicited using semantic priming tasks, using verbal stimuli (Holeomb, 1988), visual stimuli and somatosensori stimuli (Donchin, 1979; Sutton, 1979; Snyder et al. 1980).

SEMANTIC PRIMING TASKS - VERBAL STIMULI:

Neville, Kutas and Schmidt (1982a) in their ERP study of cerebral specialization during reading that the amplitude of P_{450} and subsequent positive shift at the occipital regions was larger over the hemisphere ipsilateral to the unilateral word presentations the P_{450}/is similar in some respects to P_{300} elicited by infrequent unexpected stimuli (Donchin, Ritter, and McCallum, 1978).

Very reliable alterations in the N_{100} and P_{300} components were observed elicited by words (Neville et al. 1978? Neville, 1980) greater in left hemisphere than right. ,

Neville, Kutas and Schmidt (1982b) investigated intra and inter hemispheric specialization in congenitally deaf adults during a word reading task. They found that the deaf subjects were as accurate as the hearing subjects in identifying words, however they did not display visual field assymetry.

Woodward, owens, Thompson(1990), Friedman, Simson, Ritter and Rapin (1975a) reported that P_{300} elicited by spoken

words were small/absent when subjects "merely listened" but much larger when the words were low probability, task relevent addballs. Such enhancement of P_{300} amplitude by reduced temporal probability aad task relevance is a common finding in ERP studies across a wide range of stimuli.

Cohort model (Marslen-Wilcon and Welsh, 1978; Marslen-Wilson, 1980; Marslen-Wilson and Tyler, 1980; Grosjean, 1980; Tyles, 1985) make strong prediction regarding time course of word recognition which suggested that listener identifies a word precisely as soon as he or she has sufficient information.

Further study of the timing of word recognition processes may benefit from the ability of ERP to augment mental chronomet (Kutas, McCarthy and Donchin, 1977).

In particular the latency of the P_{300} has been considered an index of stimulus evaluation time (Pritchard, 1981; Duncan-Johnson and Doachin, 1982).

Johnson, Pfefferbaum and Kopell (l985) observed that markedly broadened P_3 components, consistent with word to word,P_3 latency variability were elicited by visually presented words in a memory paradigm.

Rugg (1984a), Barrette (1990) found that ERP showed cerebral assumetry (Contingent negative variation (CNV) on phonological matching of picture names.

Kutas and Hillyard (1980) recorded ERP from subjects as they silently read 160 different seven-word sentences presented one word at a time.Substantial intersubject variability was observed in the ERP waveshapes following the words. More than half of the subjects generated P_{300} components to word stimuli which was greater in left hemisphere than right. One quarter of the sentences at random ended with a word printed in a typeface that was different from preceding words which elicited P_{300} to a greater extent.

In studies of language functioning the ERP has been reported to index perceived meaning of words (Brown, Marsh and Smith, 1973, 1976) different linguistic categorisation (Kutas and Donchin, 1979) and has been applied to the study of the development of speech perception (Molfese, Freeman and Palermo, 1975), the study of semantics (Tatcher, 1977) and study of reading (Kutas and Hillard, 1980). The extent to which ERP reliably index neurophysiological events associated with human language and cognitive functions, ERP can be of great value.

Once the spatial and temporal distribution of language-related ERP has been described in particular paradigms in normal adults, the comparision of similar paradigms from

brain damaged adults may suggest ways in which the flow of language information is altered in aphasia and in recovery from aphasia. Similar developmental studies may indicate neurophysiological changes that accompany normal and abnormal development of language abilities (Neville, 1980).

Analysis of the acoustic structures of words must precede identification of its meaning. These phases of speech processing are associated with ERP components that differed in their timing.

The differences in waveform exhibiting later negativity during semantic discrimination rather than acoustic discrimination may be related to the semantic processing of speech (Novick, Lovrich and Vaughan, 1985).

Rugg (1984, 1985) reported that ERP elicited by rhyming and non-rhyming words were differentiated by a late negative component (N_{450}) and this showed cerebral assymetry.

Barett and Rugg (1990) showed similar findings on a task involving lexical decision.

Posner and Snyder (1975a, 1975b) suggested that ERP changed when the task was automatic and attentional during lexical decision tasks.

Duncan, Johnson and Donchin (1982) recorded P_{300} latency and reaction time (RT) in a task were target letters were preceded by either a matching letter, neutral stimulus or a mismatching letter. RT and P_{300} were not later in the first two bat later in the mismatched letter.

A number of studies have reported the existence of ERP component that temporarily overlaps the P_{300} but which has a later peak (0-400 m.sec after P_{300}). In a systematic series of studies Ruchkin and Colleagues have demonstrated that P reflects initial stimulus evaluation and a component they referred to as slow wave (SW) a later more "depth" or reevaluation process that varies to task demands (Ruchkin, gutton, and Stegn, 1980b).

VISUALLY EVOKED ERP:

Rugg (1984); Ragot (1980) found visually evoked potential VEP) ie N_{160} component to be larger over the hemisphere contralateral to the visual field of stimulus exposure at all pairs of lateral electrodes. At the occipital sites only N_{160} was shorter on an average by 14 m.sec. on left hemisphere.

AUDITORY STIMULUS EVOKED ERP:

Following the germinal studies of Sutton and his colleagues (Sutton et al. 1965, 1967), it has been frequently

demonstrated that the vertex potential evoked by a task-relevant stimulus that deliver, significant information is characterized by an augmented late positive wave at about 300 m.sec. in latency (the P_3 or P_{300} component).

In one class of studies, it has been shown that an enhanced P_{300} component is elicited by a specific anticipated "target" signal that occurs unpredictably within a series of non-target stimuli and demands a special cognitive or motor response.

In the auditory modality which has received the most study, a P_{300} wave could be elicited selectively upon the detection of target signals of various types including:

1) Pitch changes (Ritter, et al. 1972? Wilkinson and Lee, 1972;Hillyard et al. 1973;,(2) Intensity shifts (Ritter and Vaughan, 1969; Picton and Hillyard, 1974),(3) Threshold level tone pips (Mast and Watson, 1968? Hillyard et al. 1971), (4) Clicks among speech sounds (Smith, et al. 1970), (5) Noise bursts among clicks (Ford, et al. 1973), (6) Omissions from a train of clicks (Picton and Hillard, 1974).

Several authors have emphasized the need for active attentiontowards the targets as a prerequisite for P_3 enhancement and have shown that ignoring the stimulus resulted in a

diminition or absence of P_{300} (Hillyard et al. 1971; Squires et al. 1973; Picton and Hillyard, 1974).

The P_{300} wave which follows the detection of an attended auditory target has a widely distributed scalp topography with maximum amplitude at central and parietal regions (Ritter, et al. 1972? Picton and Hillyard, 1974? Hillyard, et al. 1975).

P_{300} can also be elicited when the subject's attention is diverted from the auditory stimuli to read a book (Ritter et al. 1968), perform a concurrent manual task (Roth and Kopell, 1973) or simply to "ignore the sound bursts as much as possible" (Roth, 1973, Roth, et al. 1973).

PSYCHOLOGICAL CORRELATES OF P_{300}:

These results pose difficulties for any simple theoretical interpretation of the P_{300} phenomenon if it is in fact elicited by both unpredictable stimulus shifts that are being ignored and by those that are task-relevant and are being actively sought out.

Not surprisingly, then, there has been no general agreement upon how best to formulate thepsychological correlates of the P_{300}

On the one hand, the evidence that P_{300} is evoked by shifts in a non-attended train of habituating tones has led to suggestions that it is a cerebral component of the orienting response (Ritter, et al.1968; Roth, 1973; Roth and Kopell, 1973).

On the other hand, the P_3 that follows attended and task relevant stimuli has been interpreted in terms of decision making (Hillyard, 1969; Smith et al. 1970) information delivery (Sutton, et al. 1967).

Salience or significance (Sutton, 1971); Cognitive evaluation (Ritter and Vaughan, 1969), reduction of arousal (Karlin, 1970)? change in preparatory set (Karlin and Martz, 1973) and "response set" selective attention (Hillyard, et al 1973)among others.

A further unresolved question concerning the P_{300} wave concerns its latency of occurrence. Most reports place its latency within 300-450 msec, post stimulus, but some have found in as early as 210-220 m.sec. (Roth, 1973; Roth et al. 1973) and others as late as 450-550msec. (Ritter and Vaughan, 1969). Particularly puzzling are the wide discrepancies between the latencies reported for the P_{300} evoked by shifts in pitch of an irrelevant train of bursts; Ritter et al (1968)

obtained a latency of about 350 msec, in all subjects, while Roth and Kopell (1973) determined a value of 300 m.sec. and Roth (1973) found a mean latency of 217 m.sec.

Squires, Squires, and Hillyard (1975) found two distinct late positive components of the scalp recorded auditory evoked potential which differed in their latency, scalp topography and psychological correlated. The earlier component called "P_{3a} " (latency about 240 msec.) was elicited by infrequent, unpredictable shifts of either intensity or frequency in a train of tone pips whether the subject was ignoring (reading a book) or attending to the tones (counting). The later component called ^P^h" (mean latency about 350 msec) occured oniy when the subject was actively attending to the tones, it was evoked by the infrequent, unpredictable stimulus shifts regardless of whether the patient was counting the target stimuli or frequent stimuli.

Both of these are referred in literature as P_3 or P_{300}

VARIABLES AFFECTING P_{300}:

a)Attention:

Polich (1986) noted that attention was a necessary factor in the generation of P_{300} component and a decrease in attention is related to a decrease in response amplitude.

Sklare and Lynn (1984) examined the replicability of P_3 latency within subjects across measurement trials , and found only small changes from trial to trial testing during am experimental session or after several weeks.

b) Intensity:

P_{300} is considered to be an "endogenous" component because its amplitude, latency and scalp distribution does not depend upon the physical attributes of the evoking stimulus (Donchin, Ritter and McCallum, 1978).

Roth et al. (1980, 1982, and 1984) demonstrated a dependence of P_{300} amplitude on the intensity of evoking stimulus. But this study did not employ "Oddball paradigm".

Papanicolaou et al (1985) found that P_{300} amplitude was not significantly affected by the intensity of the stimulus. However statistically significant increase in P_{300} latency contingent on reduction of stimulus intensity. Hence it is important to ascertain with normal aged subjects and with clinical population, the effective stimulus intensity remains constant across the groups which are compared.

c) Frequency:

Polich, Howard and Starr (1985b) studied the frequency separation effects of target tone frequency, presence of

of masking stimulus and subjects sex on the auditory ERP using oddball paradigm. P_{300} latency became shorter (about 15 msec) as the difference between the standard (1000 Hz) and target tone frequency increased (1500, 2000, 4000 Hz) but became longer (about 10 msec.) with the presence of a white noise masking stimulus and found true with both P_{3a} and P_{3b} subcomponents

John Polich (1985) investigated factors which could affect the morphologicalquality and latency of the P_3ERP from auditory stimuli. Manipulations of attention and,

d) Probability of the target tone changed P_3 amplitude but typically demonstrated little effect on P_3 latency. Eyes open/close did not make any difference to P_3 amplitude and latency. Passively ignoring the stimulus item decreased P_3 amplitude and increased its latency relative to active stimulus discrimination. These findings support the general conclusions obtained in previous studies (Sklare and Lunn, 1984; Papani, Colaou, 1985; Polich, 1985b), P_3 latency is relatively stable and varies relatively little as a function of task variables when the subject is engaged in an explicit discrimination paradigm. Thus application of P_3 ERP should emphasize stimulus discrimination.

e) Task:

In experimental designs in which a subject either predicts prior to atrial whether/not a stimulus will be presented is guess task and in which he reports after the trial whether or not stimulus was presented is detect task. Both elicit P_{300} and no significant effect due to task is noticed on P_{300} (Ruchkin, Sutton and stega, 1980).

f) Deficits in short term memory, as well as overall memory performance are associated with both increased P_{300} latency and variability (Howard and Polich, 1985; Polich et al. 1986)

g) P_{300} latency is felt to be directly related to speed of information processing (Mullis, Holcomb, Diner and Dykan, 1985) difficulties in these areas would be reflected by longer P_{300} latencies.

h) Task difficulty:

Polich et al. (1985) observed that the stimulus discrimination ability is related to P_{300} latency with more difficult discrimination task associated with prolonged latency. P_{300} latency became shorter (about 15 m.sec) as the difference between the standard (1000 Hz) and target tone frequency increased (1500, 2000, 4000 Hz) but became longer (about 10 m.sec) with the presence of a white noise masking stimulus.

i) Sex: No differences among males and females (Polich, et al 1985).

j) Age: Peak latency is affected by aging (Brown, Marsh, LaRue 1983,) which will be discussed in detail later.

k) Prietchard (1981) cites selected attention, feedback, orienting response, language, decision confidence as other factors affecting P_{300} .

P_{300} AS CLINICAL TOOL:

The P_{300} or P_3 component of the ERP is beginning to demonstrate considerable utility as a clinical tool for the assessment of cognitive function.

Although the neurophysiology underlying P_{300} is still being explored (Halgren, et al. 1980; Odaka et al.1983), the cognitive events associated with its generation have received considerable attention (Donchin, 1981; Donchin, Ritter and McCallum, 1978; Prietchard, 1981). Because P_{300} is thought to reflect stimulus evaluation and classification processes, it has found application in the assessment of cognitive function.

Initial applications found that latency of the P_{300} becomes longer with an increases in adult age (Goodin, et al.

1978b; Syndulko et al. 1982; Brown et al. 1983; Pfefferbaum, et al. 1984a; Picton et al. 1984; Polich, et al. 1985a).

It also increases substantially with mental dysfunction such as mental retardation (Squires et al. 1979) and dementing illness (Brown et al. 1982; Goodin et al.1978a; Hansch, et al. 1982; Lai et al. 1983; Pfefferbaum et al. 1984b; Polich, et al. 1986).

Additional studies have suggested that shorter P_{300} latencies are associated with relatively superior memory performance in neurologically normal subjects (Polich, et al. 1983; Howard and Polich, 1985).

Changes in P_{300} component can originate from fluctuations in cognitive state (Goodin et al. 1983) amount of alcohol typically consumed (Polich, 1984? Polich and Bloom 1986) and individual differences in memory retrieval (Kavis, et al. 1984).

Auditory Processing Disorders:

Neville, Kutas and Schmidt (1982, a, b) studied P_3 and related long latency components and various learning and developmental processes in adults and children (using both normal hearing and deaf subjects, examined intra and

inter hemisphere specialization daring reading activities and found that visual BRP were sensitive to cortical activities occuring during the processing of written language material. Furthermore they demonstrated that ERPs were useful in defining differences in cortical organisation occuring between the normal hearing and deaf subjects during reading activities.

Satterrfield, Schell, Backs and Hidaka (1984) working with hyperactive and normal boys, observed significant latency and amplitude difference between these groups using auditory ERPs. They noted that younger hyperactive subjects exhibited, longer peak latency and smaller amplitude while the older clinical subjects showed shorter latency and larger amplitude.

Satterfield, Schell and Backs (1987), reported on the results of a longitudinal investigation of both delinquent and nondeliquent hyperactive boys as well as normal age and gender matched controls. The authors found that latency measures of the auditory long latency response were sensitive to abnormalmaturational changes in the nondelinquent group when compared to both the delinquent and normal subjects, airsa and Clotz (1990) also found P_3 latency delay and decreased amplitude in children with auditory processing disorders when compared to matched normal group.

Cognitive functions:

Auditory ERPs were also studied by Finley, Faux, Hutcheson and Amstutz (1985) to study children with cognitive disorders. They found that compared to normal controls, children with organically confirmed cognitive problem had significantly delayed P_{300} latency. In addition children with organic disorders could be differentiated from those with functional disorders or psythiatric disorders on basis of P_{300} latency. Thus patients who may appear demented but are actually depressed have normal P_{300} latencies while patients with dementia have abnormal P_{300} latency.

In addition to distinguishing pseudodementia from dementia, it seems to provide a sensitive indicator of fluctuations in mental state experienced by individual Patients as a result of changes in underlying illness (decrease in P_{300} latency with clinical improvement in mental functions and decrease P_{300} latency in clinical deterioration).

Unlike the routine sensory evoked potential latencies that may remain abnormal even when function has been restored, the P_{300} latency seems to reflect dynamic aspects of cognitive function in neurologic illnesses that affect cognitive function.

Goodin, Squires, and Starr (1978) found P_{300}, latency increases of the demented patients was significantly increased over the normal and neurologically impaired subjects due to cognitive dysfunction occuring in dementia. Significant amplitude decrease of P_{300} was found between normal and demented patients but amplitude measurements were considered insensitive for the determination of information processing.

Leppler and Greenberg (19) found that P_{300} latency in dementia supported finding of Goodin et al (l978) P_{300} latency could not separate mildly demented patients from normal. Mild and moderate could be separated (arterosclerotic dementia) and also moderate and normal ie. P_{300} latency was sensitive enough to separate patients with dementia of the same etiology at different stages of the disease.

Goodin, Starr, Chippendale and Squire (1983) found findings correlating with study of Finley, Faux, Hutsceson and Amstutz (1985).

Polich (1984) found that peak latency taken at P_2 recording site was negatively correlated with the amount of alcohol typically consumed and hence subsequent cognitive declined.

Polich et al (1986) found P_{300} latency longer in patients with primary degenerative dementia and other cognitive impairment compared to age matched controls. Also found P_{300} latency reflects the degree of cognitive decline in dementing illness.

Language and motor speech disorders:

Evaluating children with either confirmed language or motor speech disorders Mason and Mellor (1984) observed significant intra and inter hemispheric amplitude differences in the auditory long latency response compared to normal controls. They speculated these findings may prove beneficial in the examination of various factors involved in normal language development.

Long P_{300} latency have been seen in autistic subjects (Niwa# ct al* 1983* Courchesne, 1984).

Musiek (1989a) has also speculated that the P_{300} would be beneficial in the evaluation of individual with aphasia or related communication disorders, since generation of the P_{300} required that an individual understand the task at hand, Musiek feels that observation of the ERP gives important information regarding receptive capabilities which would be useful in planning a therapeutic program.

In considering all of the above, it seems apparent that,of all electrophysiological measures the LLP, including the ERP may be most sensitive to behavioural or cognitive problems within the CNS (Polich, 1986; Polich, et al.1986). While many of these process are often observed in children with central auditory processing disorders (CAPD), there is little published information specifically examining the auditory P_{300} or associated long latency component (LLC) in children with auditorily confirmed processing disorders such as described by Willford and Burleigh (1985).

EXPONENTIAL ELECTROPHYSIOLOGICAL AGING - P_3 LATENCY:

All of the late potentials are influenced by nearo-maturational factors with Nl, P2 and N2 thought to stabilize by about 10-15 years of age (Kilney, 1985? Mason and Mellor, 1984; Musiek, et al. 1988).

The P_{300} component appears to mature somewhat later them the earlier waves with several studies showing a decrease in latency and an increase in amplitude from ages 5-16, followed by a progressive decrease in amplitude and an increase in latency throughout adulthood (Courchesne, 1978? Goodin, Squires and Henderson, 1978; Pfefferbaum, Ford, Roth and Kopell, 1980; Polich, Howard and Starr, 1985) and aging (Goodin et al. 1978).

ERP have been accorded while performing Steaberg's paradigm (1966) of memory retrieval task by young (Roth et al. 1975; 1977; 1978; Gomer, et al. 1976; Adam and Collins, 1978) and young and old subjects (Marsh, 1978; Anders et al. 1972; Anders and Fozar,1973; Ford et al. 1979) and found P_{300} increased with increasing memory sets and age and thus P_{300} reflects the time it takes to encode the test stimulus evaluation of stimulus. They also found same relation with RT but this included response processes also.

This is consistent with research of (Kutas, et al.1977; Squires, et al.1977; Duncan-Johnson,1978; Roth et al. 1978) indicating that generation of P_{300} is related to the processes associated with stimulus evaluation and that the latency of P_3 reflects the relative time taken to evaluate stimulus sufficiently to perform the task.

Pfefferbaum, et al (1980) found that the older subjects differed from the younger ones in severa/respects - P_3 amplitude at P was smaller,P_3 latency and RT were greater and relationship between P_3 latency and RT was considerably altered.

The recent reports of the clinical utility of ERP in the diagnosis of dementia (Goodin et al.1978a) and in the demonstration of less profound cognitive deficits (Pfefferbaum,

et al. 1979a) give promise of an expanding role for clinical evoked potential applications.

However in order to use the late components of the ERP as a clinical tool, the alterations due to "normal" aging must be well established. This is especially important for the study of cognitive impairment as the major alteration seen in dementia - prolongation of P_3 latency is also seen, but to a lesser degree in normal aging (Goodin et al. 1978b).

The latencies of AEP component occuring after 150 m.sec. (P2, N2, P3) have all been shown to increase as a function of age (Marsh and Thompson, 1972; Beent, et al 1977; Goodin et al.1978b; Ford, et al.1979; Pfefferbaum, et al. 1979b).

In contrast components occuring before 150 m.sec. whow little or no latency change with age (Goodin et al.1978b; Pfefferbaum, et al. 1979b) amplitude of these earlier components occuring after 125 m.sec. have been reported to decrease in amplitude with age (Dustman and Beck, 1966; 1969; Luders, 1970; Brent, et al. 1977). Goodin et al. (1978b) also found a decrease in amplitude of a derived N2-P3 complex with age.

Pfefferbaum et al (1979b) reported an increase in the baseline to peak amplitude of the positive components (P1 and

P2) to a sustained auditory stimulus which was ascribed, at least partially to a diminution of the sustained potential (sp).

Goodin et al (1978b) demonstrated that the later the evoked potential component with regard to stimulus onset time, the more it is prolonged with age (ie P_3 is prolonged more than P2 which is prolonged more than Nl). They calculated the slope of the regression line for the latency of the various components on age to be 1.8 m.sec/year for P_3, 0.7 m.sec./year for P2 and 0.1 m.sec/year for Nl.

Pfefferhaum et al.(1980) found P2 was larger and later, P_{300} later and had a different scalp distribution and SW was smaller in the elderly. While the older subjects in this study were remarkably healthy and intellectually active, the presence of occult CNS pathology causing mild, undetected deterioration of cognitive functioning cannot be ruled out. Also the fact that normal aging and dementia both produce a prolongation of P_{300} latency raises the question of similarity in the mechanism and warrants further examination of the ERP changes associated with each process In dementia, P_{300} is prolonged when comparision is made to age matched norms, thus the P_{300} latency prolongation is

over and above that produced by aging alone. The earlier occuring component, P2, however is aot affected in this manner in dementia. Normal aging is accompanied by an increase in both P2 and P_{300} latency. Dementing processes produce a further increase in P_{300} which is additive to the age related prolongation bat does not affect P2 latency. The authors say that both aging and dementia prolong P_{300} but pattern of change is different.

Brown, Marsh and LaRue (1983) found that while P_{300} latencies of depressed patients have not differed significantly from the age P_3 regression line of normals, most demented patients have P_3 latencies 2 or more standard Deviation (SD) longer than their age peers. They also found longer P_3 latency were associated with lower Mini mental status scores correlations of both P_{300} latency and the mini mental status (MMS) with age in these patients were not significant. These data indicate P_{300} latency is a reliable measure of the degree of cognitive impairment in the geriatric patients.

A single exception to age Vs P_{300} latency increase reported by Michaellweski et al (1982) for the emitted P_{300} to mixing clicks in which no age differences were seen for N2 and P3 latency for other traditional or latency

corrected average. Linear increase in P_3 latency beginning at puberty and astending into VIIIth decade have been reported (Goodin, et al. 1978b; Squires et al. 1980; Syndulko, et al. 1982; Polich, et al. 1984).

All studies report significant positive linear correlations, with slopes ranging from 1.1 m.sec/year (Syndulko et al. 1982) to 1.8 m.sec./year (Goodin et al. 1978b). The single exception to the finding of a linear P_3 latency increase with age is reported by Beck et al. 1980) who found an increase Of 0.8 m.sec/year between ages of 28 and 63 and 1.6 m.sec/year between 63 and 79 years.

Brown, Marsh and Lame (1983) have replicated findings of above study with regard to the effects of age on amplitude and latency of ERP components. Additionally they found age/ERP component latency relation is nonlinear. The age P_3 latency slope for subjects under 45 years is 0.53 m.sec/year vs. 3.14 m.sec/year for the subjects over 45 years. Their data are best fitted with a curvilinear first and second degree orthogonal polynomial which describes a positively accelerating latency increase with age. If the function is assumed to be linear and is intact non-linear (as found), there are two potential consequences for the recognition of deviant P_{300} latency and use of this result in the detection

of dementia. For the oldest subjects, deviance would be overestimated because a linear regression line fitted to the comparison group would not reflect the accelerating P_{300} latency in normal individuals within the 60-80 age range. For subjects in the middle age range (approximately 35-55) years) an inappropriate linear function would underestimate the degree of P_{300} latency deviance and consequently the incidence of dementia. A non linear relation between age and P_{300} latency ought to be considered say the authors in building norms for use in clinical evaluation.

Pfefferbaum, et al. (1984a) studied subjects age range 18-90 years for P_{300} in both auditory and VERP and found a significant increase in P_{300} latency with age of 1-1.5 m.sec/ year. The range of normal P_{300} latency for a given age (1 standard error of the regression = 40 msec) for VEP) was much larger than obtained by other investigations. The VEP produced higher P_{300} latency-age correlation than auditory paradigm. There was also an apparent change in the scalp topography of P_{300} with age (distribution becoming unilateral distribution in older age from parietal distribution in young).

Pfefferbaum et al. (1984b) used this normative data on P_{300} to distinguish dementia depression and schizophrenia and

found P_{300}- RT correlation distinguishes better rather than P_{300} alone.

Picton et al. (1984) recorded ERP from Fz normal subjects (20-79 years). The latency of P_{300} wave to auditory stimuli increased regularly with increasing age at a rate of 1.36 m.sec. per year and its amplitude decreased at a rate of 0.18 /uv per year. Similar age related changed in P_{300} wave occured in the visual and somatosensory modalities. The change in the latency of the P_{300} wave occured independently of any change in the RT which showed not age related change. The latency of P_{300} wave associate with the detection of an omitted auditory stimulus did not change significantly with age.

Sklare and Lynn (1984) studied normative aspects and within subject variability for neurologically and audiologically normtalyoung adults aged 22-34 years across test essions separated by 2-4 weeks (M=9) and across trial within one test session (M=20). A strong positive correlation was present between latency of test session I and II. ANOVA was not significant as a function of either tests or trials for test-retest groups. ANOVA was significant between trails within one session, the small mean latency

difference between trials (4.7 msec) interpreted as being clinically unimportant. The stability of P_{300} latency found in this study over a period of 2-4 weeks supports itsapplication to the study of normal and disordered cognitive processes.

Holcomb, Diner and Dykman (1985) studied visual stimuli to elicit ERP in 108 normal subjects ranging in age from 8-90 years. Age related inferences were found for both P_{300} latency and amplitude. Children and elderly adults were found to have latest P_{300} and earliest P_{300} were found in subject in their twenties. A curvilinear function best described P_{300} latency - age relation. P_{300} decreased in amplitude at posterior site and increased in frontal locations with increasing age.

Gordon, et al, 1986) found P_3 latencies of normal subjects and regressed on their ages and resulting linear equation was used to predict normal latency at a given age (15-89) and then identify cases of dementia. Curvilinear regression analysis they found the prediction of a normal P_{300} latency at Cz considered to be best on the basis of $Y=0.45x + 307$ for subjects less than 63 years (standard errors = 26) and $Y = 2.3lx+190$ (standard errors = 38) for subjects greater than 63 years. Also they revealed the increase in latency accelerated between ages

60-80 age range. Thus they gave equation until age 63 and after and one below. Also demented patients could be identified accurately.

Picton et al (1986) studied 10 elderly females (Mean = 69.1 years) and 10 young females (Mean = 22.6 years) to assess interaction between age and discrimination difficulty. The P_{300} was significantly later for the more difficult discrimination and was significantly greater later for the older subjects than for the young. However, there was no significant interaction between age and difficulty. Their results indicate that the age related changes in the latencies of AEP were independent of discrimination difficulty.

Because of its relationship to information processing the P_{300} has been studied extensively across the lifespan in order to evaluate the neurophysiological basis of the charges in cognition that occur with aging. Normal increase with age in P_3 latency/cognitive processing time might be due to a decrease in neural conduction velocity caused by an age related decrease in myelination.

However, further studies of the relationship between P_{300} latency and age are needed to clarify whether these

interpretations and findings are right and to establish reliable normative P_{300} data. Such research must investigate large number of older aged persons because P_{300} latency appeals to be extremely variable in the elderly (Pfefferbaum, 1978). Some elderly people have latency comparable to those aged 20 years or some very delayed.

"Perhaps the greatest potential of P_{300} components investigations is not simply to establish P_{300} latency measures as diagnostic aid. Any other psychological tast can identify dementia and other disorders. Rather investigations of P_{300} responses in dementia, aging etc may further our understanding of which aspects of cognitive functions are affected by these states especially dementia".

In the future auditory evoked responses battery may include the cognitive component P_{300} which may be used to monitor progress in patients with central nervous system impairment following various habilitative interventions. More information may be derived with multiple electrode placements. As the imaging techniques become more and more sophisticated, there may be better correspondence between specific sites of lesions and results of event related potential studies.

!METHODOLOGY

The present experiment was undertaken to study the following objectives:

1. If there is any differences in the P_{300} latency and P_{300} amplitude of normals and geriatrics.
2. If there is any difference in the P_{300} latency and P_{300} amplitude of geriatrics between groups 50-60 years and 60-70 years.
3. To find if age can be used topredict the latency of P_{300} ie to find age P_{300} regression line in normal and geriatrics and find if a linear or curvilinear aquation can be used to predict normal latency at a given age.

SUBJECTS:

Three groups of subjects were tested. The first group consisted of 16 normal adults between age range of 18-22 years(8 males and 8 females) with mean age of 19.8 years who were doing undergraduate training in Audiology and Speech therapy at All India Institute of Speech and Hearing. The second group consisted of 10 geriatrics, between age range 50-60 years (7 males and 3 females) with mean age of 53.8 years. The third group consisted of 10 geriatrics

between age range 50-70 years (9 males and 1 female) with mean age of 65.4 years.

The groups were not cautiously matched on gender as the review revealed no gender effect on the auditory cognitive potentials (Polich, 1986c).

CRITERION FOR SELECTION OF SUBJECTS:

1. All subjects had volunteered for this experiment.
2. None of the subjects had any past history of any otological involvement and psychological disturbances.
3. All the adult subjects were preselected on the basis of hearing within 25 dB HL (ANSI 1969) on air-conduction threshold at frequencies 250, 500, 750, 1KHz, 2 KHz, 4 KHz and 8 KHz bilaterally with airbone gap not exceeding 10 dB HL bilaterally.
4. All the geriatric subjects were preselected on the basis of hearing within 25 dB HL (ANSI 1969)on Air conduction threshold at frequencies 250, 500, 750, 1 KHz, 2 KHz, 4 KHz and 8 KHz bilaterally with airbone gap not exceeding 10 dB HL bilaterally.
5. All the subjects did not report of any history of noise exposure, giddiness or tinnitus.
6. All the subjects did not report or any medical or neurological impairment such as hypertension, essential tremors etc.

7. The subjects were able to relax in the presence of electrodes placed for the duration of testing and impedance values were within normal limits.
8. All the subjects had no previous exposure to cognitive potential recording.

As it was difficult to find normal geriatrics with normal hearing no associated medical problems like diabities, hypertension, incidental sampling was done.

INSTRUMENTATION:

The entire experiment was conducted in a specially designed electrically isolated and air conditioned sound treated room using Nicolet Compact Auditory System 2 channel electrodiagnostic system equipped with J.Version (1986) evoked potential software. TDH-39 earphones with telephonic comporation P/N cushions were used to deliver the condensation tone burst stimuli (both target and non-target) of particular frequency(2 KHz) for the target sound and 750 Hz for nontarget standard tone at 75 dB HL binaurally at probability ratio of 80/20 for non-target/target. The rate of presentation was 0.7/sec. with a rise and fall time of 2 m.sec. and a plateau of 20 m.sec. binaurally. The amplifier filter were set to a band pass of 1 Hz - 30 Hz.

The parameter of non-target stimulus S1 were Frequency = 750 Hz; Intensity = 75 dB; Probability rate = 80%. The parameter of target stimulus S2 were Frequency = 2 KHz; Intensity = 75 dB; Probability rate = 20%. The equipment set up, patient record test selection were done as given in the manual.

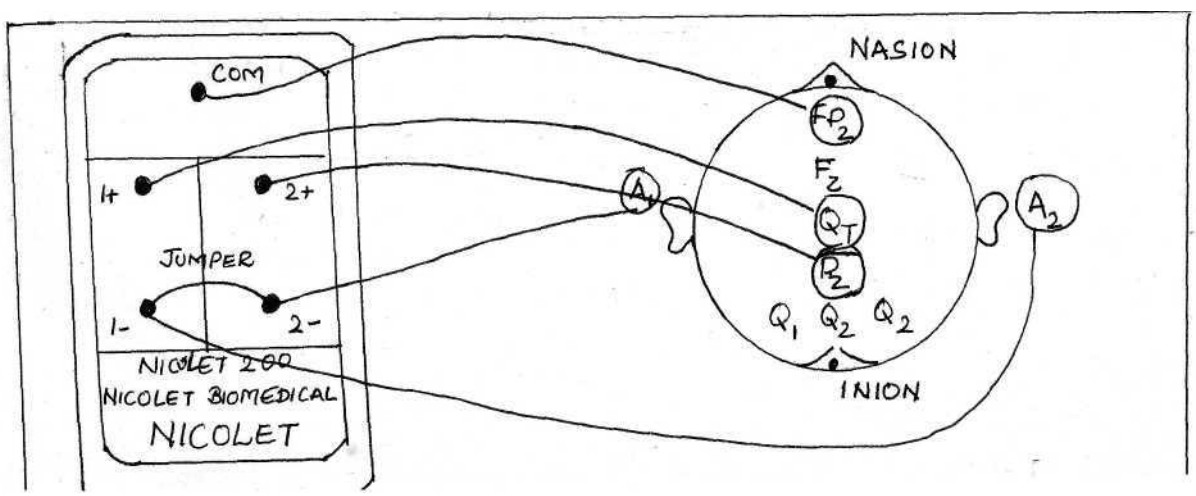
ELECTRODE PLACEMENT:

The electrode site for two channel mapping recordings were selected as C_Z and P_Z, as positive, the FP_Z as common and Al and A2 as negative.

The electrodes were plugged into the following jacks of the electrode head box.

Site	Headbox connection
Forehead (FP_z)	CON
Vertex (C_z)	1+
P	2+
Left ear (Al)	1-
Right ear (A2)	

ELECTRODE CONNECTION FOR A P_{300} RESPONSE:



Silver cup electrodes were fixed at the sites given in Fig.l after thorough skin surface cleaning with spirit and later filled with standard EEG electrode paste, suitably secured in place with surgical tapes. In all the recording maximum of 10% automatic artifact rejecting were" allowed.

PATIENT SET UP:

The patient was reclining or sitting comfortably with the head fully supported to ensure noise free recordings. Neck and jaw muscles were relaxed and in a comfortable position.

INSTRUCTIONS TO THE SUBJECTS:

1. The subjects were instructed to be alert but relaxed throughout the recording
2. The subjects were asked to keep his/her eyes open and to fixate his/her vision to one spot to minimise alpha interference.
3. The subjects were asked to relax all neck and jaw muscles.
4. The subjects were told they would hear two stimuli. The difference between the rarely occuring stimulus and frequently occuring stimulus was described. Here they were told a low pitch click would occur frequently and a hi-pitch click would occur rarely.

5. The subjects were asked to pay maximum attention and to count the number of rare occuring stimuli silently and ignore the frequent none target stimuli.
6. The subjects were cautioned to avoid time locked physical responses such as eye blinks with each presentation of the rare stimulus.

PROCEDURE OF RECORDING:

1) The earphones were placed on the subjects ear, being careful not to dislodge any electrodes.

2) The blue earphone was over the left ear and the red earphone over the right ear. The center of the earphone diaphragm was placed directly over the ear canal opening. This is not always the most comfortable earphone placement, but this placement is critical for the delivery of accurate stimulus intensity levels.

The electrode leads and electrode head box were as far away from the earphones as possible. The earphones and head box cables did not overlap.

MEASURING IMPEDANCE:

The impedance of the electrodes were measured for each electrode for two channels. The impedance values for the positive and negative electrodes were referenced to the common electrode.

All electrode impedances were less than 5 K and within 3k of each other. They were adjusted to read this value.

The negative electrodes Al and A2 were linked together by means of a jumper to obtain the clearest P_{300} waveform after the impedance measurements were made.

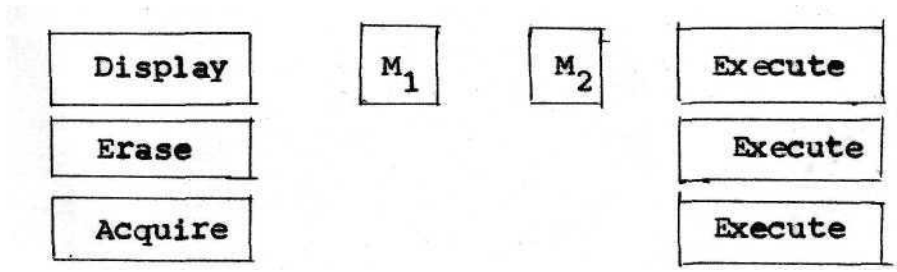
MEMORY BLOCKS:

The P_{300} recording was done by collecting the responses to the frequent stimulus and responses to the rare stimulus in separate memory blocks which were contiguous.

PROCEDURES! FOR ACQUIRING DATA:

Once the patient was settled, data was acquired. The status of S1 and S2 were observed to see if all parameters were appropriate.

The P_{300} responses were displayed with, the response to the frequent stimulus in memory block 1 on the left and responses to rare stimulus memory block 2 on the right. The system is activated by pressing in sequence.



The averaging process begins now and waveform became visible after a few minutes of averaging.

The amplitude of Electro encephalograph (EEG) was within the vertical screen boundaries. If the EEC exceeds the screen, the sweep was rejected and the word artifact would appear on the screen. The number of seeeps accepted (NA) and the number of sweeps rejected (NR) for s1 and S2 were displayed on the lower portion of the screen. If more than 10% rejection rate was displayed, the patient was resettled making sure that all head and neck muscles were relaxed.

Averaging was stopped after 300 artifact free sweeps were acquired.

The waveforms were then centered on the screen using baseline correction (BLS) command, base line corrects all displayed waveforms by removing any direct current(DC) offset.

The gain of the waveforms were adjusted pressing the gain button arrows.

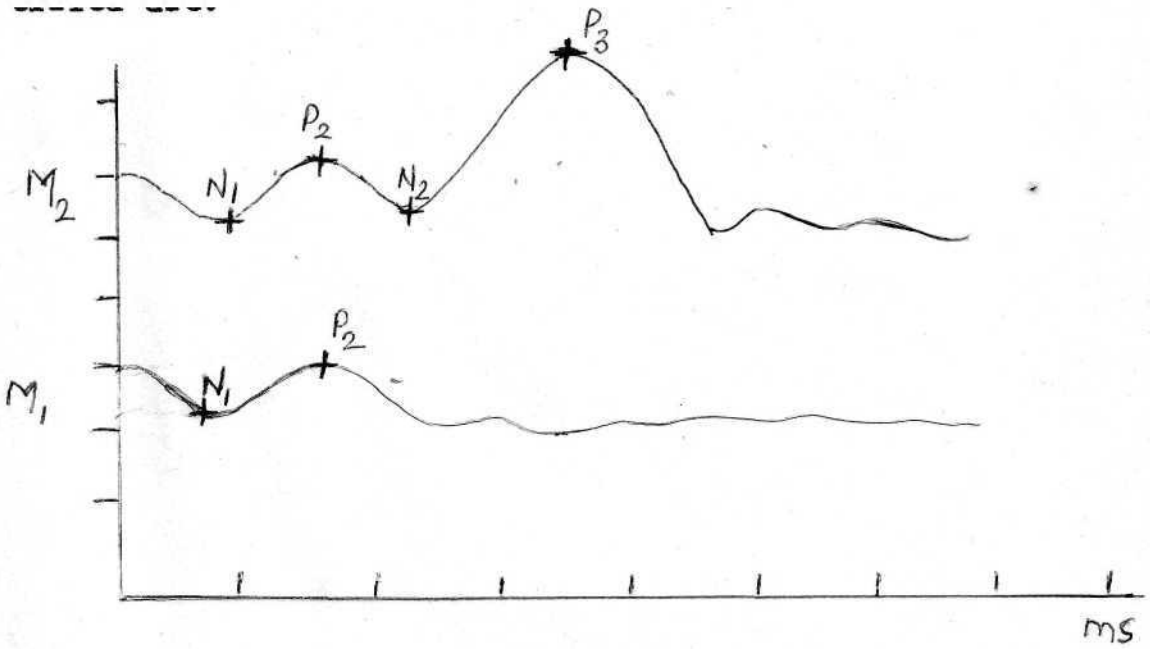
PROCEDURE FOR ARCHIVING DATA:

Storing data: After the patient record was created, the data was stored using datafile name. The data was then recalled and plotted.

LABELING WAVE FORMS:

The identification (IDN) command was used to identify and label waveforms amplitudes and latencies. This information was also printed and stored.

An example of waveform latencies and amplitudes identifi
are:



Frequent		Rare
N1 = 92.80	N1	= 102.4
P2 = 172.8	P2	= 163.2
Amp - P2= 8.59	N2	= 198.4
		Amp - 82 = 10.15
		P3 - 352.00
		Amp P3 = 15.42

The latency of P_3 was defined by the computer at each recording site as the most positive peak after 250 m.sec. of the average waveform to the target tones. Its amplitude was measured from base line to peak. This base line was defined for each participant as the average voltage of 100 m.sec. epoch prior to the onset of each stimuli (Gorden, Krauschen, Starfield, Meares and Howson, 1986).

The above measures were done for each subject of both the normal young adult group and the geriatric group and the values of the two were compared. The results obtained were analysed using statistical procedures to find out if there was statistically significant delay in latency as a function of aging.

ANALYSIS, RESULTS AND DISCUSSION

The data of P_{300} latency amplitude measures were subjected to statistical analysis.

Descriptive statistics was applied to find the mean, median and standard deviation of P_{300} amplitude and latency of each of three groups.

Mann Whitney two sample U test was carried out between each of three groups and between normal adult group and geriatric group as a whole.

Linear regression analysis was done between age and P_{300} latency. .

Table-1: Statistical summary group-1 age-18-22 years.

Variable	No.of subjects.	Mean	Median	SD	Minimum	Maximum
Age	16	19.79	20	1.48	18	22
N_1	16	100.69	99.2	9.67	89.6	123.2
P_2	16	171.6	172	17.83	147.2	206.4
Amp P_2	16	6.02	6.05	3.75	.14	12.3
N_1	16	98.06	99.2	7.84	76.8	108.8
P_2	16	165.65	164.8	14.34	140.8	187.2
N_2	16	211.43	210.4	26.81	158.4	252.8
Amp P_2	16	9.82	11.13	4.09	2.63	18.35
P_3	16	317.31	320.8	19.04	272	337.6
Amp P_3	16	5.18	5.46	3.11	.39	11.32

Frequent

Table-2: Statistical Summary groug-2 age 20-60 Years . 54							
Variable		No.of sub-jects	Mean	Median	SD	Minimum	Maximum
	Age	10	53.8	53.5	3.49	50	59
Fre quent	N_1	10	100.24	98.40	18.89	76.8	132.8
	P_2	10	192.16	196.8	17.01	169.6	222.4
	Amp.P_2	10	9.60	9.27	2.17	0.15	12.5
Rare	N_1	10	100.96	95.2	18.05	72	129.6
	P_2	10	176.24	179.6	15.17	153.6	201.6
	N_2	10	236.72	234.8	20.11	208	265.6
	Amp P_2	10	10.26	11.71	3.36	5.17	13.86
	P_3	10	333.04	340.8	24.74	292.8	390.4
	Amp P_3	10	8.10	7.96	4.15	2.53	12.89

Table-3: Statistical group-3 Age 60-70 years.

Variable		No.of subjects	Mean	Median	SD	Minimum	Maximum
	Age	10	65.4	65.5	2.98	60	69
Fre quent	P_1	10	96.99	100	12.71	73.6	118.75
	P_2	10	181.92	190.8	29.83	136	231.25
	Amp P_2	10	9.28	8.98	4.02	3.9	15.4
Rare	N_1	10	100.13	95.2	21.87	72	150.4
	P_2	10	169.4	162.4	26.03	139.2	204.8
	N_2	10	222.56	235.6	32.72	160	268.75
	Amp P_2	10	6.93	7.37	2.17	3.51	10.15
P_3		10	357.96	353.1	43.68	302.4	440
	Amp P_3	10	9.01	9.32	4.79	2.44	18.55

Table-4: Statistical summary group I & II combined, Age 50-70 years

Variable	No.of sub-jects	Mean	Median	SD	Minimum	Maximum
Age	20	59.6	59.5	6.74	50	69
Fre-quent N_1	20	98.62	99.2	15.72	73.6	132.8
P_2	20	187.04	194.4	20.21	136	231.25
Amp P_2	20	9.44	9.08	3.15	3.9	16.4
Rare N_l	20	100.55	95.2	19.52	72	150.4
P_2	20	172.82	173.6	21.03	139.2	204.8
N_2	20	229.64	227.6	27.41	160	268.75
Amp P_2	20	8.60	8	3.24	3.51	13.86
P_3	20	350.5	340.8	35.39	292.8	440
Amp P3	20	8.58	8.84	4.39	2.44	18.56

RESULTS AND DISCUSSION:

The statistical analysis of the data on P_{300} obtained is given in Table-1 in terms of mean, median and standard deviation.

1. There was a significant difference on Mann Whitney twosample test between normal adults (18-22 years Mean 19.8 years) and aged Group-2 (50-60 years. Mean 54 years) for P_3 latency (Z = -3.1034 P 0.001) and P_3 amplitude (Z= -1.8 P 0.06).

2. There was significant difference between normal adults (18-22 years, Mean 19.8 years) and 3rd group (60-70 years Mean 65.4 years) for P. latency. (Z = -2.16 at P .05) and P_3 amplitude at (Z = -2.1079 P .05)

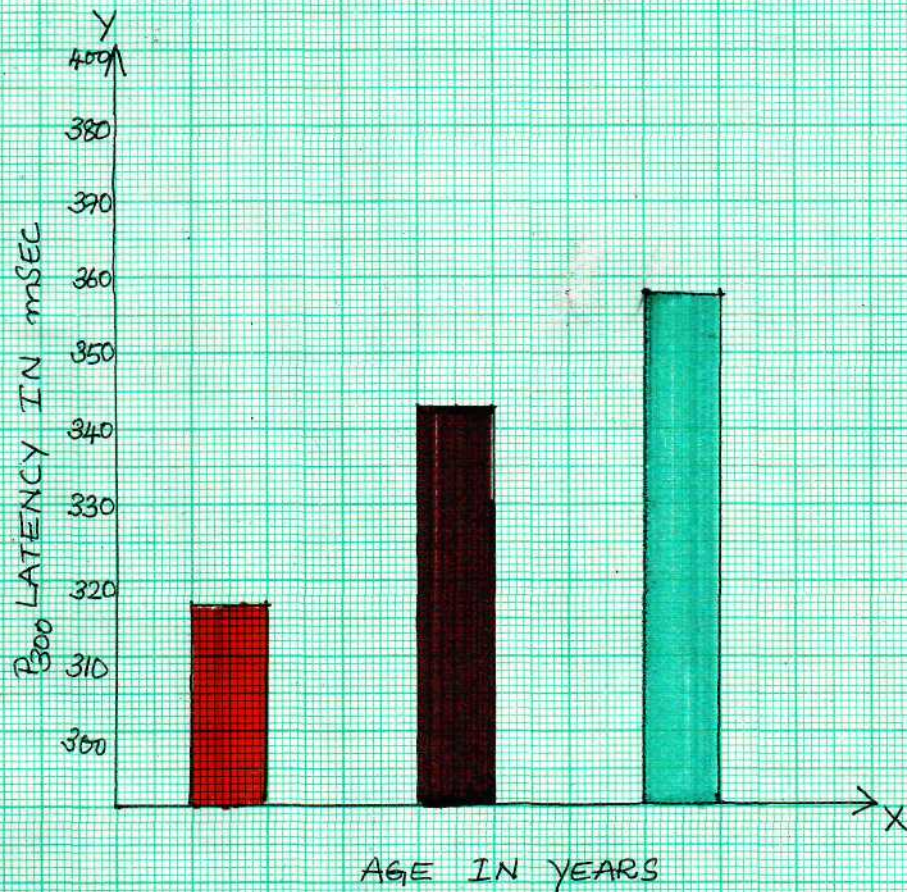
3. There was significant difference between normal adults (18-22 years; Mean 19.8 years) and geriatrics (50-70 years; Mean 59.8 years) for P_3 latency (z = -3.11 at P , 0.001) and P_3 amplitude (Z= 2.3270 at P .05).

These results indicate that there is age related significant variation in the latency of P_{300} on comparing geriatrics (50-70 years) and adults (18-23 years) and (2) there is age related variation in amplitude of P_{300} on comparing geriatrics (50-70 years) and adults (18-22 years). Since P_{300} amplitude is highly variable and dependent on other variable than age this finding is not of importance.

4. There was no significant difference between 2nd and 3rd group ie between geriatrics (50-60 years) and 60-70 years for P_{300} latency and amplitude. This indicates there is no age related significant variation in geriatrics of 50-60 ages and 60-70 ages for P3QQ latency and amplitude.

5. Correlation results of Spearman's rho showed no significant correlation between age and P_3 latency. On linear regression neither linear function nor curvilinear function could approximate the P_{300} latency and age relationship.
6. There is greater variability in 60-70 age range SD=43.68 than 50-60 SD =24.74 and young adults SD = 19.04.

FIG. 1: MEAN P_{300} LATENCY OF THE THREE AGE GROUPS



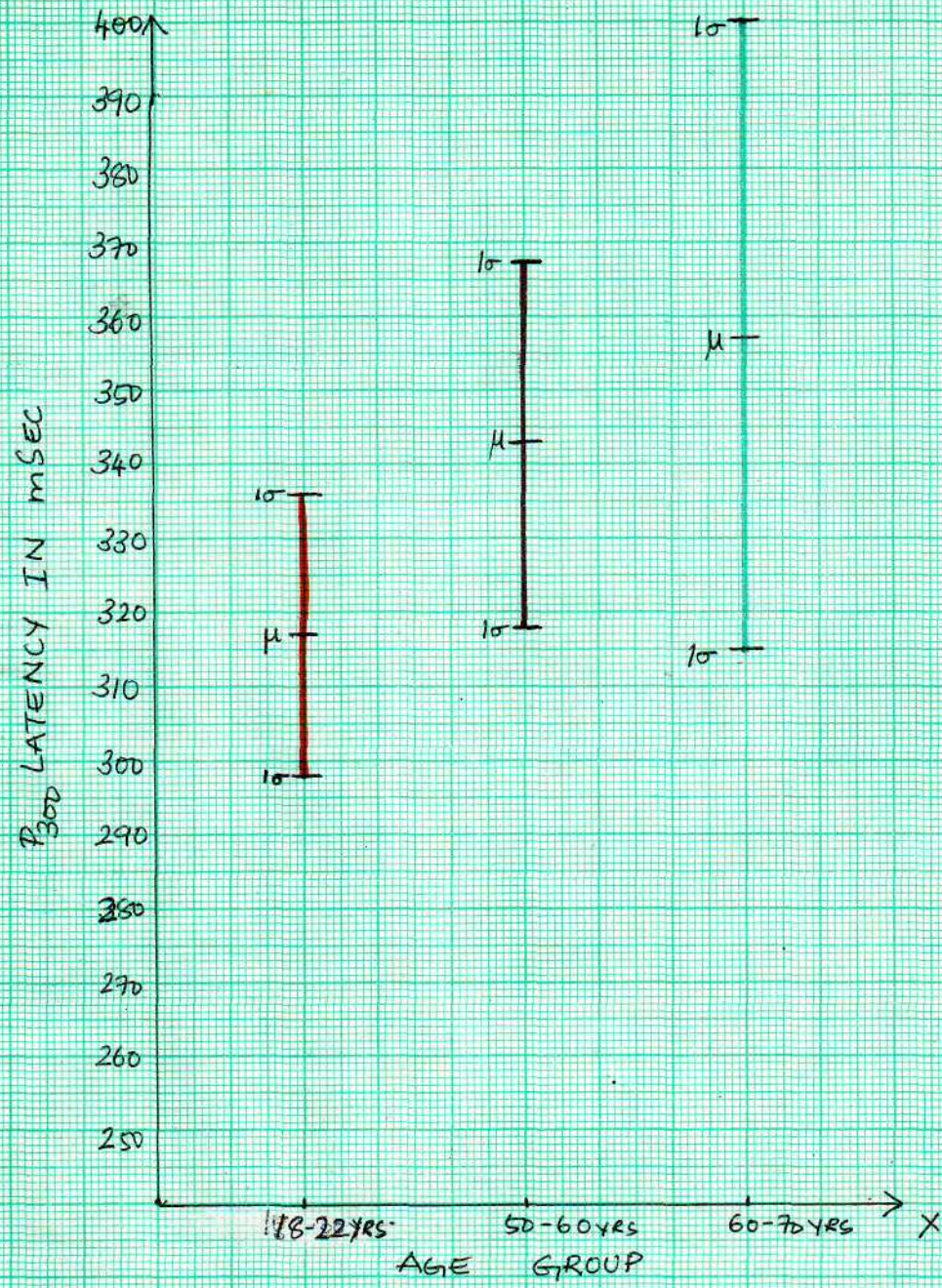
KEY:

- AGE GROUP 18-22 YEARS
- AGE GROUP 50-60 YEARS
- AGE GROUP 60-70 YEARS

SCALE

Y AXIS – 1 UNIT = 10 mSec

FIG: 2 – 15 D VARIATION IN THE THREE AGE GROUPS



KEY:

– 1σ VARIATION OF AGE GROUP – 18-22YRS

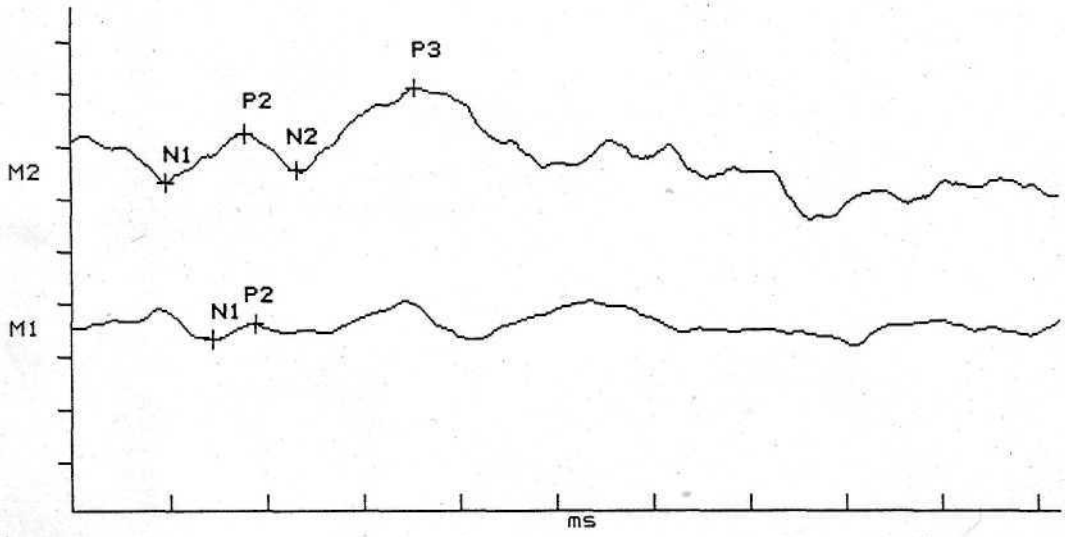
1σ VARIATION OF AGE GROUP – 50-60YRS

1σ VARIATION OF AGE GROUP – 60-70YRS

SCALE:

Y AXIS – 1UNIT = 10mSec.

P_{300} WAVEFORM OF A SUBJECT AGED 18YRS



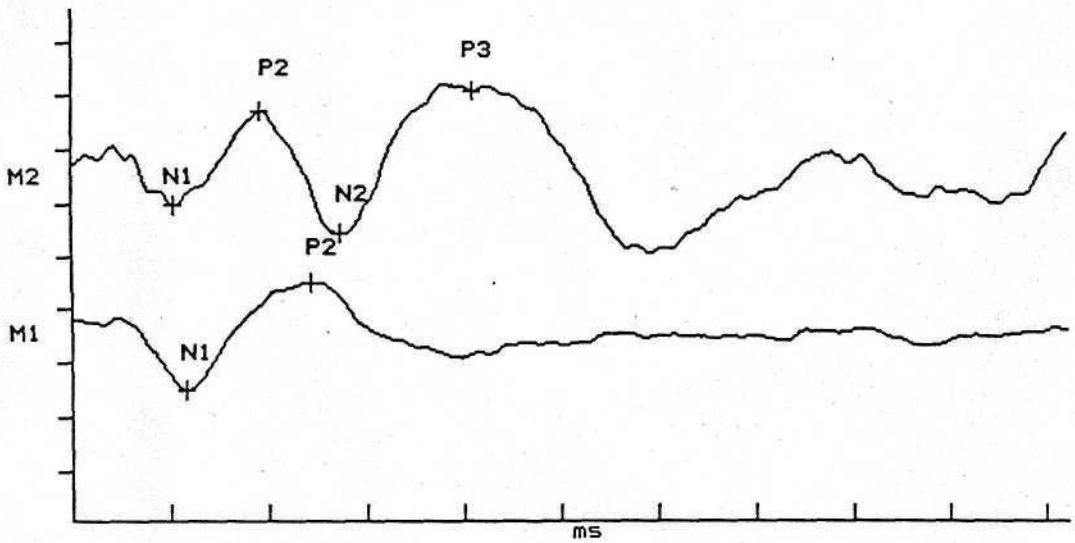
P300

	FREQ	RARE	
N1	115.20	N1	76.80
P2	150.40	P2	142.40
AMP-P2	1.36	N2	185.60
		AMP-P2	4.29
		P3	283.20
		AMP-P3	7.22

M	AMP/DIV	ms/DIV	TESTTIME	REMARK	OFFLINE ROUTINE
1	4.88 uV	80.0	19:13:22		
2	4.88 uV	80.0	19:13:22		

	AQT		STIM			AMP		AUD LEFT							AUD RIGHT						AUD NOISE		
M	TIME	SWP	RATE	DUR	SNS	LFF	HFF	TYPE	POL	CAL	LEV	RAM	PLA	FREQ	TYPE	POL	CAL	LEV	RAM	PLA	FREQ	TYPE	DEV	LEV
	ms		/s	us	uV	Hz	Hz				dB							dB						dB
1	800	240	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	750	TONE	CON	nHL	70	2ms	20ms	750	OFF	OFF	0
2	800	60	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	2K	TONE	CON	nHL	70	2ms	20ms	2K	OFF	OFF	0

P_{300} Waveform Of A Subject Aged - 52 yrs



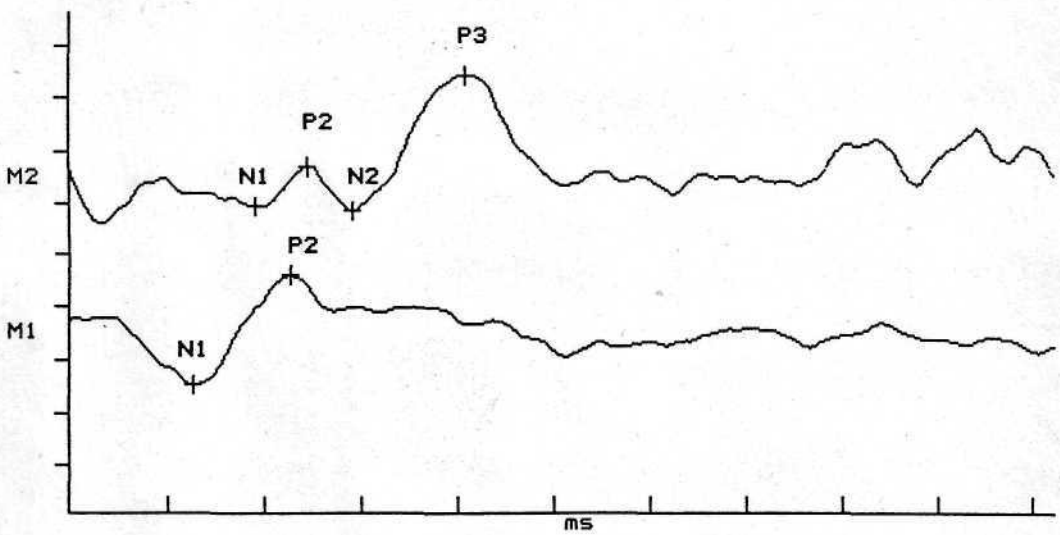
P300

FREQ		RARE	
N1	92.80	N1	83.20
P2	195.20	P2	153.60
AMP-P2	9.37	N2	219.20
		AMP-P2	8.00
		P3	328.80
		AMP-P3	12.30

M	AMP/DIV	ms/DIV	TESTTIME	REMARK	OFFLINE ROUTINE
1	4.88 uV	80.0	10:8:17		
2	4.88 uV	80.0	10:8:17		

M	ACT		STIM		AMP			AUD LEFT							AUD RIGHT							AUD NOISE		
	TIME ms	SWP	RATE /s	DUR us	SNS uV	LFF Hz	HFF Hz	TYPE	POL	CAL	LEV dB	RAN	PLA	FREQ	TYPE	POL	CAL	LEV dB	RAN	PLA	FREQ	TYPE	DEV	LEV dB
1	800	239	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	750	TONE	CON	nHL	70	2ms	20ms	750	OFF	OFF	0
2	800	61	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	2K	TONE	CON	nHL	70	2ms	20ms	2K	OFF	OFF	0

P300 Waveform of a Patient Aged-65 yrs



P300

FREQ		RARE	
N1	100.80	N1	152.00
P2	180.80	P2	195.20
AMP-P2	9.76	N2	232.00
		AMP-P2	3.51
		P3	326.40
		AMP-P3	11.91

M	AMP/DIV	ms/DIV	TESTTIME
1	4.88 uV	80.0	16:44:30
2	4.88 uV	80.0	16:44:30

REMARK

OFFLINE ROUTINE

	AQT		STIM			AMP		AUD LEFT							AUD RIGHT						AUD NOISE		
M	TIME ms	SWP	RATE /s	DUR us	SNS uV	LFF Hz	HFF Hz	TYPE	POL	CAL	LEV dB	RAM	PLA	FREQ	TYPE	POL	CAL	LEV dB	RAM	PLA	FREQ	TYPE	DEV	LEV dB
1	800	238	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	750	TONE	CON	nHL	70	2ms	20ms	750	OFF	OFF	0
2	800	62	0.7	100	100	1	30	TONE	CON	nHL	70	2ms	20ms	2K	TONE	CON	nHL	70	2ms	20ms	2K	OFF	OFF	0

Table-5: Studies on P_{300} and normal aging.

	N	X P_3	SD	X Age	SD	Correlation	Slope in m. sec/ year
All subjects							
Brown et al	49	322	37.6	45	21.7	.648	1.12
Polich et al	77	331	37.0	43	17.6	.610	1.28
Syndulko et al	45	351	35.5	48.2	19.7	.645	1.16
Goodin et al	40	337	37.6	39.3	17.3	.853	1.85
Sklaire -and Lynn	20	306.8	16	27.1	4.37	.56	2.01
Pfefferbarum et al	135	—	—	18-90		.32	1.5
Gordon et al	55	-	—	15-89	6.7	.55	
Present study	36	335.7	35.5	-	6.7	NC	-
Young subjects 45							
Brown et al	25	304	22.7	25.8	8.2	.193	.53
Polich et al	41	310	24.7	29.2	7.6	-082	-.27
Syndulko et al	20	330	27.2	29.7	8.9	-.012	-.20
Goodin et al	28	318	22.9	29.4	8.3	.614	1.69
Present study	16	317.34	19.03	19	1.47	NC	NC
Older subjects ' 45	-						
Brown et al	24	342	40.5	65.3	9.3	.720	3.14
Polich et al	36	354	35.0	59.7	9.8	.435	1.56
Syndulko et al	25	368	32.1	63.0	11.4	.632	1.77
Goldin et al	12	381	26.5	62.2	8.9	.471	1.40
Present study	20	350.5	35.3	59.6	6.7	NC	

N - Indicates number of subjects

X/P_3 - Indicates mean P_{300} latency in msec.

SD - Indicates standard deviation.

X age - Indicates mean age

NC - Indicates no correlation.

R - Indicates range

The findings 1, 2, and 3 are in concurrence with other studies done on the same topic as shown in the Table.5.

While finding 4 and 5 do not agtee with other studies of similar nature as shown in the Table-5.

The first three findings indicate that older subjects differed from the younger one in P_3 amplitude and P_3 latency (Goodin, 1975; Pfefferbaum, et al.1980). But P_3 amplitude data show great variance and dependent on extraneous variables hence is not given importance.

Also these findings provide a normative data for P_3 latency and for younger age group (18-22 years) and older age group (50-70 years). This is especially important for the study of cognitive impairment as the major alteration seen in dementia ie prolongation of P_3 latency is also seen but to a lesser degree in normal aging as shown by this study (Goodin, et al 1978b).

Findings 4 and 5 indicate that we were not able to establish any significant positive correlation between age and P_3 latency.

The review of literature an this aspects reveals that there are several contradictions regarding this aspect.

While Goodin et al (1978b); Polich et al (1982); Syndulko et al (1982) found significant positive linear correlation between age and P latency.

Brown et al (1982) found that age P_3 latency relation was non-linear. The slope of age P_3 latency for subjects under 45 is 0.53 m.sec/year vs. 3.14 msec./year for subjects over 45 years.

Gordia et.al. (1986) established curvilinear function between age and P_3 latency for subjects less than 63 and greater than 63.

Picton (1986) study indicated that the age related changes in the latency of AEP were independent of task difficulty. Hence the linear vs non-linear function must await further experiments,specifically designed to study these issues.

Thus these differences of regression may be due to variety of factors including paradigms, task instructions P_3 latency measurement technique and differences in subject population.

In the present study, the nature of the task might have tapped elements of task strategy and mental ability in a way that enhanced individuals differences and therefore diminished the association of P_3 latency and age.

Of relevance here is the fact that our subject population was incidentally sampled and included individuals representing a broad range of socio economic status and educational attainment. Thus individual differences in P_3 lateney attributable to factors other than age were perhaps maximised.

In contrast other studies (Goodin et al (1978); Brown et al(l983) used a more homogenous, higher socio-economic population drawn largely from hospital personnel and retirement community.

Thus there may be some variable related to subject selection that at times brings out a linearity, other time curvilinearity and other time no linearity in the age P_3 latency regression.

In summary, the results of this study reaffirm the role of aging as a contributing factor to changes in both the latency of the P_3 component.

This study is in contrast to some others which reported P_3 -age regression linearity, differences in task demands, patient samples and ERP analysis technique might explain some of the discrepancy.

SUMMARY AND CONCLUSIONS

The current study was undertaken to investigate if there was any age related significant variation in the latency of P_{300} and its amplitude on comparing normal young adults (18-22 years) and normal geriatrics (50-70 years). It was also designed to determine the most accurate description of the relation between P_{300} latency and age on age P_{300} latency regression.

Three groups of normal volunteers subjects were tested. The I group 16 normal adults (18-22 years), the II group, 10 normal geriatrics (50-60 years) and third group (60-70 years), 10 normal geriatrics participated in this study. They were studied on an "auditory oddball paradigm" in which infrequently securing target and non-target events were used to elicit event related potentials with a prominent P_{300} component. Regularly occuring auditory stimuli (750 Hz, 70 dB, 80% of trials) was randomly replaced with tone of different pitch (2000 Hz, 70 dB, 20% of trials). The subjects were instructed to keep a cumulative count of rate tones and to ignore frequent tones. P_{300} was recorded at Cz and Pz electrode sites.

The mean P_{300} latency was 317.31 m.sec. (range 272-337.6), 340.8 (range 292.8-390.4) and 357.96 (range 302.4-440)-msec. for the I, II and III group respectively.

There was a significant difference between -

1. means for P_3 latency for group I normal adults (18-22 years) and group II geriatrics (50-60 years) (Z= -3.10 P .001)
2. means for P_3 latency for group I normal adults and group III geriatrics 60-70 years (-2.16 at P .03).
3. means for P_3 latency for group I normal adults and group II and III combined geriatrics 50-70 years (Z =-3.11 at P .001).

There was no significant difference for P_3 latency between group II (50-60 years) and group III (60-70 years). Age P_3 latency regression showed no correlation, neither linear nor curvilinear.

The results of this study reaffirm the importance of aging as a contributing factor to changes in the latency of P_{300} component.

This study is in contrast to some others which reported P_3 - age regression linearity/curvilinearity/nonlinearity differences in task demands; patient samples and ERP analysis technique might explain some of the discrepancy.

SUGGESTIONS FOR FURTHER RESEARCH:

1. To carry out similar study on large number of normal adults and geriatrics.
2. To vary other parameters like intensity, frequency and frequency space between the target and non-target stimuli and carry out similar experiment.
3. To carry out studies on P_{300} in the handicap population like dementia, learning disability, language and motor speech disorders, mental retardation, etc.

BIBLIOGRAPHY

Adorn, N., and Collins, G.I. (1978): "Late components of the visual evoked potential to search in short term memory". Electro.enceph. Clin. Neuro. Physiol. 44, 147-156.

Anders, T.R., Fozard,J.L.,and Lillyquist, T.D. (1972): "Effects of age upon retrieval from short term memory". Develop. Psychol. 6, 214-217.

Anders, T.R., and Fozard, J.L., (1973): "Effects of age upon retrieval from primary and secondary memory". Develop.Psychol. 9, 411-416.

Barette, E.S., Rugg, M.D., (1990): "Event related potential and phonological matching of picture names". Brain and Language, 38, 424-431.

Beck, E.C., Swanson, C., and Dustman, R.E.,(1980): "Long latency components of the visually evoked potential in man - effects of aging". Exp. Aging. Res., 6, 523-545.

Begleister, H.D., Porjesz, B., Bihari, B.,and Kissin, B., (1984): "Event related potentials in boys at risk for alcoholism". Science, 225, 1493-1495.

Brent, G.A., smith, D.D.B., and Michaeleski, H.J. (1977): "Differences in the evoked potential in young and old subjects during habituation and dis-habituation procedures". Psychophysiology, 14, 96-97.

Brown, W.S.,Marsh, J.T.,and Smith, D.B.T. (1973):Cited in "Word to word variation in event related potentials component latencies spoken words" by Woodward,S.H(Eds), Brgin and Language, 38, 488-503.

Brown, W.S., Marsh,J.T.,and Smith,D.B.T. (l976):Cited in "Automatic and attentional processing - A event related brain potential analysis of semantic priming", Holcomb,P.J.(Ed), Brain and Language, 35, 66-65, 1988.

A.

Brown, W.S., Marsh, J.T., and LaRue/(1982): "a event related potentials in psychiatry: differentiating depression and dementia in the elderly". Bull, Los Angeles, Neurol.Soc. 47, 91-107.

Brown, W., Marsh, J.T., Larue, A. (1983): "Exponential electrophysiological aging: P3 latency". Electroenceph.Clin. Neurophysiol. 55, 277-285.

Buchbaum, M.S. (1974): "Average evoked response and stimulus intensity in identical and fraternal twins", Physiol. Psychol, 2, 365-376.

Courchesne, E. (1978): "Neurophpyiological correlates of cognitive development: Changes in long latency Event related potential from childhood to adulthood". Electroenceph. Clln. Neuro physiol, 45, 468-482.

Cournesne, E. (1984): "Cognitive component of event related brain potentials: Changes associated with development" In 'tutorials in event related potentials research: Endogenous components', A.W.K.Gaillard, and W.Ritter (Ed), 329-344, North Holland Amsterdam.

Davis, H., Engebretson, E.L., Lowell, T,, Mast, J., Sauterfield, and Yoshi, N. (1964): "Evoked responses to clicks recorded from the human scalp". An "Handbook of clinical audiology"3rd Ed. Ed. Jack Katz.

Donchin, E., Hitter, W., and McCallum, W.C. (1978): "Cognitive psychophysiology: The endogenous components of the event related potentials". In "Event related brain potentials In man". Eds. E.Callaway, et al. Academic Press, New York, 349-441.

Donchin, E. (1979): "Event related brain potentials: A tool in the study of human information processing" In 'Evoked brain potentials and behaviour' Ed. H.Begleiter, Vol.2, Plenum Press, New York, 13-88.

Donchin, E. (1981): Surprise ... Surprise? Psychophysiology, 18, 493-513.

Duncan-Johnson, C.C., and Donchin, E.(1977): "On quantifying surprise: The variation of event related potentials with subjective probability". Psychophysiology, 14, 456-467.

Duncan-Johnson, C.C. (1978): "The P300 component of the cortical event related potential as an index of subjective probability and processing duration". Doctoral dissertation. University of Illinois, Champagn Vebana, III, 1978.

Duncan-Johason, C.C., and Donchin, E. (1982): "The P300 component of the event related brain potentials as an index of information processing". Biological Psychol. 14, 1-52.

Dustman, R.E., and Beck, E.C. (1966): "Visually evoked potentials: Amplitude changes with age". Science, 191, 1013-1015.

Fif6r, R., and Sierra-Irizarry, B. (1988): "Clinical applications of the auditory middle latency response". Am.J.Otol, 9, 47-56.

Finley, W.W., Faux, F.s., Hutcheson, J., Amstutz, L. (1985): "Long latency event related potentials in the evaluation of cognitive function in children". Neurology, 35, 323-327.

Ford, J.M., Roth, W.T., Dirks, S.J. and Kopell, B.S.(1973): "Evoked potential correlates of signal recognition between and within modalities". Science, 181, 465-466.

Ford, J.M., Roth, W.T., Mohs, R., Hopkins, W, and Kopell, B. S. (1979): "Event related potentials recorded from young and old adults during a memory retrieval task". Electroenceph. Clin.Neurophysiol. 47, 450-459.

Friedman, D., Simson, R., Ritter, W., and Rapin (1977): "CNV and P300 experimental paradigms for the study of language". In. J.E.Desmedt (Ed) "Language and Hemispheric specialisation in man: Cerebral BRPS progress in Chin.Neurophysol. Vol.3, Basel, Krager Press, 205-211.

Grosjean (1980): Cited in "Word to word variation in event related potentials component latencies spoken words" Ed. Woodward, S.H., Owens, J., and Thompson, L.W. Brain and Language, 38, 388-503.

Gomer, F.E., Spicuzza, R.J. and O'Donnell, R.D. (1976): "Evoked potential correlates of visual item recognition during memory scanning tasks" Phvsiol. Psychol. 4, 61-65.

Goodin, D., Squires,K., Henderson, B., and Starr, A. (1978a): "Age related variations in evoked potentials to auditory stimuli in normal human subjects". Electroenceph. Clin.Neuro physiol. 44, 447-458.

Goodin, D.s., Squires, K.C., and Starr, A. (1978b): "Long latency event related components of the auditory evoked potential in dementia" Brain, 101, 635-648.

Goodin, D.S., Starr, A., Chippendale, J., Squires, K.C. (1983): "Sequential changes in the P3 component of the auditory evoked potential in confusional states and dementing"illnesses". Neurology, 33, 1215-8.

Gordon, E., Kauchin, C., starfield, P., Meares, R., and Howson, A. (1986): "Prediction of normal P3 latency and diagnosis of dementia". Neuropsychologia, 24, 823-830.

Grossberg, S., (1980: "How does the brain build a cognitive code?" Psychological Review, 87, 1-51.

Hall, J.W. (1989): "New clinical applications of sensory evoked responses in audiology" Paper presented at the Annual convention of the North Carolina speech, hearing and language association, Charlotte, Nc, March, 1989.

Halgren, E., Squires, N.K., Wilson, C.S., Rohrbaugh, J.W., Babb, T.L., and Crandall, P.H.(1980): "Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events" Science, 210, 803-805.

Hanhen, H.C., Syndulko, K., Cohoen, S.N., Goldberg, Z.I., Potnin, A.R., and Tourtelotte, W.W. (1982): "Cognition in parkinson disease: An event related potential perspective". AnnJNeurol. 11, 599-607

Hillyard, S.A.(1989): "The CNV and the vertex evoked potential during signal detection: A preliminary report". In Average evoked potentials: methods, results and evaluationm Ed. E. Donchin, and D.B.Lindsley, MASA, Washington, D.C. 349-353.

Hillyard, S.A., Squires, K.C., Bauer, J.W., and Lindsay, P.H. (1971): "Evoked potential correlates of auditory signal detection". Science, 172, 1357-1360.

Hillyard, S.A., Hirk, R.F., Schwent, V.L., and Picton, T.W. (1973): "Electrical signs of selective attention in the human brain". Science, 182, 177-180.

Hillyard, S.A., Courcesnne, E., Krausz, H.I. and Picton, T.W. (1975): "scalp topography of the 'P3' wave in different auditory decision task" in Event related slow potentials of the brain, Eds. W.C.McCallum, and J.R.Knott, John Wright and Sons, Bristol.

Hoffmeister, F, Cited in "Brain function in old age evaluation of changes and disorders". Eds.F. Hoffmeister, C.Nuler and H.P.Krause, Springler-verlag, Berlin Heidelberg, New York. 1979.

Holecomb, D.T.(1988): "Automatic and attentional processing: An event related potential analysis of semantic priming". Brain and Lang. 35, 60-85.

Howard, L., and Polich, J. (1985): "P300 latency and memory span development" Develop.Psychol. 21, 293-289.

Jerger,J., Oliver, T., and Chimet,R. (1988): "The auditory middle latency response". Semin.Hear, 9, 75-85.

Jirsa, R.E., Clontz, K.B. (1990: "Long latency and event related potentials from children with auditory processing disorders". Ear and Hearing, 11, 222-232.

Johnson, Pfefferbaum, and Kopell (1935) Cited in "Word to word variation in event related potentials component latencies spoken words" Ed. Woodward, S.H., Owens, J., and Thompson, L.W., Brain and Language, 38, 488-503.

Karlin, L. (1970): "Cognition, preparation, and sensory-evoked potentials" Psychol. Butt. 73, 127-136.

Karlin, L., and Martz, Jr. M.J. (1973): "Response probability and sensory evoked potentials" In. s. Korn Blum (Ed), Attention and performance, IV, Academic Press, New York, 175-184.

Kavis, D., Fabiani, M. and Donchin, E. (1984): "P300 and memory: Individual differences in the Resteroff effect" Cognition Psychol. 16, 177-216.

Kileny, (1982): Cited in "Word to word variation in event related potentials component latencies spoken words", Eds. S.H.Woodward, Owens, J., and Thomson, L.W. Brain and Language, 38, 488-503.

Kilney, P., Robertson, C.M.T. (1985): "Neurological aspects of infant hearing assessment".J.Otolarynqol. 14 (Suppl.14), 34.

Kutas,M., McCarthy, G., and Conchin, E. (1977): "Augmenting mental chronometry: The P300 as a measure of stimuibus evaluation time".science , 197, 792-795.

Kutal and Donchin (1979): Cited in "Word to word variation in event related potentials component latencies spoken words" Ed. Woodward,S.H., Oweens, J., and Thompson, L.W., Brain and Language, 38, 488-503.

Kutas,M., and Hillyard, S.A.(1980): "Reading senseless sentences: Brain potentials reflect semantic in congruity'" Science, 207, 203-205.

Laccy, B.C., and Lacey, J.I. (1980): "Cognitive modulation of time dependent primary bradycardia" Psvchophvsiology, 17, 209-221.

Lai, J.A., Brown,W.S., Marsh, J.T., and LaRue, A.(1983): "Covariation of P3 latency and mini mental state scores in geriatric patients". Psychophysiologyy 20, 455.

Leppler, G.J., and Greenberg, J.H. "Speech and Hearing centre. The Brooklyn Hospital, Brooklyn, New York, and Communication Science Laboratory, Bowling, Green State University, Bowling Green, Ohio,

Luders, H. (1970): "The effects of aging on the waveform of the sotnatosensory cortical evoked potential". EEC and Chin Neurophysiol, 29, 450-460.

Marsh, G.R. , and Thompson, L.w. (1972): "Age differences in evoked potentials during an auditory discrimination task" Gerontalogist, 12, 44, 1972

Marsh, G.R. (1972): "Age differences in evoked potential correlates of a memory scanning process". Exp. aging Res, l, 3-16.

Marslen-Wiison, W. , and Welsh, A. (1978): "Processing interaction during word recognition in continuous speech", cognitive psychology, 10, 29-63.

Marslen-Wiison, W. (1980): "Speech understanding as a psychological process". In J.C.Simon (Ed.) Spoken Language generation and understanding, Dardrecht Reidel

Marslen-Wilson, W. , and Tyler, L. (1980): "The temporal structure of spoken language understanding". Cognition, 8, 1-71.

Mast, T.E., and Watson, C.S. (1968): "Attention and auditory evoked responses to low detectahillty signals". Perception Psychophys. 4, 237-240.

Mason, S.M. , and Mellor, D.H. , 31984): "Brainstem, middle latency and late cortical evoked potentials in children with speech and language disorder". Electroenceph.Clin.Neurophysiol, 59, 297-309.

Michaelewski, H.J, , Patterson, J.V. , Bowman, T.E. , Litzlemar, D.K. , and Thompson, L.W. (1982): "A comparison of the emitted event related potential in older and young adults", j.Genetolooy, 52-58.

Molfese, D.F. , Freeman and Palerno (1975): cited in "word to word variation in event related potentials component latencies spoken words", woodward, et al (Ed): Brain and Language, 38, 488-503.

Molfesie, D.P. (1978): "Neuroselective correlates of categorical speech perception in adults". Brain and Language, 5, 25-35.

Molfesie, D.F. (1979): "Cortical involvement in the semantic processing of co-articulated speech cues". Brain and Lang. 7, 86^100.

Mullis, R.J. , Holomb,D.J. , Diner, B.C., and Dykman, R. A. (1985): "The effects of aging on the P300 component of theVERP". Electroenceph Clip. Neurophysiol. 62, 141-49.

Musiek, F.E. , and Baran,J.A. (1987): "Central auditory assessment". Thirty years'of challenge and change. Ear and Hearing, 8, 225-365.

Musiek, F.E. , Verket, S.B. , and Gollegly, M.A. (1988): "Effects of neuromaturation on auditory evoked potentials". Seminars in Hearing, 9, 11-15.

Musiek, F.E. (1989a): "Late potentials as P300: Paper presented at the symposium on electrophysiological measurement". Verbana, IL, august, 1989a.

Neville, H.J. , Snyder, E. , Knight, R. , and Galambos, R. (1978): Event related potentials in language and non-language tasks in patients with Alexia without agraphia" in D.Lehman and E.Callaway (Eds), Human Evoked Potentials, New York, Plenum Press, 269-283

Neville, H.J. (i960): "Event related potentials in neuropsychological studies of language". Brain and Language, 11, 300-318.

Neville, H.J, Kutas, M. , and Schmidt, A* (1982a): "Event related potential study of cerebral specialization during reading: X studies of normal adult". Brain and Language, 3, 3OO-315.

Neville, H.J. , Kutas, M., and Schmidt, A. (l982b): "Event related potential study on congenltally deaf adults". Brain and Language, 10, 316-337

Novick, B. , Lourich, w. , and Vaughan, S. (1985): "Event related potentials associated with the discrimination of acoustic and semantioaspect of speech" Neuropsychologia, 23, 87-1O1

Okada, Y.G., Kaufman, L., and Williamson, S.J. (1983): "The Hoppocampal formation as a source of the slow endogenous potentials". Electroenceph. Clin. Neurophysiol. 55, 417-426.

Papanicolaou, C.A., Loring, W.D., Raz, N., Eiseaberg, M.H., (1985): "Relationship between stimulus intensity and the P300" Psychophysiology, 22, 3, 326-329.

Pfefferbaum, A., Horvath, T.B., Roth, W.T. and Kopell, B.s. . (1979a): "Event related potential changes in chronic alcbbolis". Electroenceph. Clin. Neurophysiol. 47, 637-647.

Pfefferbaum, A., Ford, J.N., Roth, W.T., Hopkins, III, W.P. and Kopell, B.s. (1979b): "Event related potential changes in healthy aged females". Electroenceph. Clin.Neurophysiol, 46, 81-66.

Pfefferbaum, A., Ford,J.M., Roth, W.T., and Kopell, B.g. (1980a); "Age differences in P3 - reaction time associations". Electroenceph Clin.Neurophysiol. 49, 257-265 .

Pfefferbaunt, A., Ford, J.N., Roth, W.T., and Kopell, B.S. (1980b): "Age related changes in auditory event related potentials". Electroenceph. Clin.Neurophysiol. 49, 266-276.

Pfefferbaum, A., Ford,J.M.m Wenegrat, B.G., Roth, W.T., and Kopell, B.S. (1984a, b): "Clinical application of P3: I Normal aging. II. Dementia, depression and Schizophrenia". Electroenceph. Clin.Neurophysiol. 59, 85-103; 104-123.

Picton, T.W.,and Hillyard, S.A., (1974): "Human auditory evoked potentials II: Effects of attention". Electroenceph.Clin.Neurophysiol. 36, 191-1993.

Picton, T.W., Hillyard, S.A., Kraus, H.I., Galambos, R.(1974): "Human auditory evoked potentials I:Evaluation of components". Electroencephalograph Clin.Neurophysiol. 36, 179-190.

Picton, T.W., Woods, D.L., Baribeau-Braun, J., Healey,T.L. (1977): "Evoked potential audiometry", J.Otolaryngol., 6, 90-119.

Picton, T.W., stuss, D.T., Champagne, S.C., and Nelson, R.F.(1984): "The effects of age on human event related potentials". Psychophysiology. 21, 312-326.

Picton, T.W., Cerri, A.A., Champagne, C.S., Stuss, T.D., and Nelson, F.R. (1986): "The effects of age and task difficulty on the late positive component of the auditory evoked potential". Cerckera Psychophysiology: Studies in Event Related Potentials (EBG.Suppl.38), 1, 30.

Polich, J., and Starr, A. (1983): "Middle late and long latency auditory evoked potentials"in Moore, E.J.(Ed.) Bases of auditory Brain stem evoked responses, Grune and Stratton Inc, New York.

Polich, J., Howard, L., and Starr, A. (1983): "P300 latency correlates with digit span". Psychophysiology, 20, 665-669.

Polich, J. (1984): "P300 latency reflects personnel drinking history SPR Abstracts, 1984.

Polich, J., Howard, L.A., and Starr, A.(1985a): "Effects of aging on the P300 component of the event related potential from auditory stimuli: Peak definition, variation and measurement". J. of Gerontology,

Polich,J., Howard,L., and Starr, A. (1985b): "stimulus frequency and masking as determinants of P300 latency in event related potentials from auditory stimuli". Biological Psychology, 21, 309-318.

Polich, J. (1985b): "Attention probability and task demands as determinants of P300 latency from auditory stimuli". Electroenceph.Clin. Neurophysiol, 63, 251-359, 1986.

Polich (1986): "Normal variation of P300 from auditory stimuli" . Electroenceph. Clin.Neuropsychol. 65, 236-240.

Polich,J., Ehlers,L.C.S Otis, S., Mandell, J.A., Bloom,E.F. (19867: "P300 latency reflects the degree of cognitive decline in dementing illness". Electroencephalogra. Clin.Neurophysiol. 63, 138-144

Polich,J., and Burn, T.(1987): "P300 from identical twins". Neuropsychologica, 25, 299-304.

Posner, M., and Sayder, C.R.R. (1975a): "Attention and cognitive control" in R.L. Solse (Ed.) Information processing and Cognition, The Loyoco Symposium Hillsdale, New Jersey, Erlbaum.

Posner, M., and Snyder, C.R.R.(1975b): "Facilitation and Inhibition inthe processing of signals" In PMA Rebbit and s.Domle (Eds), Attention and Performance, New York, Academic Press.

Price, R.L., and Smith, D.B.D. (1974): "The P3oo wave of the averaged evoked potential: A bibliography". Physiological Psychology, 2, 387-391.

Pritchard, W.s. (1981): "Psychophysiology of P300"psychol. Bull. 90, 506-540.

Ragot, R., Renault, B. and Remond, A. (1980): "Hemispheric involvement during a binaural reaction time task P300 and motor potential" In Progress in brain research", H.H.Korrnluber and L. Decke (Ed.), Vol.54, 661-667, Elsevier, Austcrdam.

Regan, D. (1972): "Evoked potentials in psychology, sensory physiology and clinical medicine". London, Chapman and Hall.

Ren, M.A., Schwartz, M. (1976): "Retinal versus central processes in determining averages evoked response waveforms". Physiology and Behaviour, 16, 705-709.

Ritter, W., Vaughan, Jr. H.G., and Costa, L.D. (1968): "Orienting and habituation to auditory stimuli: A study of short term changes in average evoked responses". Electroenceph.Clin. Neurophysiol., 25, 550-556.

Ritter, W., and Vaughan, Jr.H.G., "Average evoked responses in vigilance and discrimination: A reassessment". Science, 164, 326-328.

Ritter, W., Simson, R., and Vaughan, Jr. H.G. (1972): "Association cortex potentials and reaction time in auditory discrimination". Electroenceph.Clin. Neurophysiol. 33, 549-55.

Roth, W.T. (1973): "Auditory evoked responses to unpredictable stimuli". Psychophysiology, 10, 125-137.

Roth, W.T., and Kopel, B.S.(1973): "P300 - an orienting reaction in the human auditory evoked response". Percept. Motor Skills, 36, 219-225.

Roth, W.T., Kopell, B.s., Tinklenberg, J.R., Darley, C.P., Sikora, R. and Vesecky, T.B. (1975): "The contingent negative variation during a memory retrieval task". Electroenceph.Clin. Neurophysiol. 38, 171-174.

Roth, W.T., Ford, J.M., and Kopell, B.S., (1978): "Long atency evoked potentials and reaction time". Psychophysiology, 15

Roth, W.T., Horvath, T.B., Pfeffertaum, A., Tinklenberg, T.R., Mezzich, J.E., and Kopell, B.S. (1979): "Late event related potentials and schizophrenia". In H.Begleiter (Ed.). Evoked brain potentials and behaviour. Vol.2, Plenum Press,New York, 499-515.

Roth, W.T., Tinklenberg, J.R., and Kopell, B.s. (1979): "Ethanol and Marihuana effects on ERA in a memory retrieval paradigm". Electroenceph. Clin.Neurophysiol. 42, 321-388.

Roth, W.T., Doyle, C.M., Pfefferbaum, A., and Kopell, B.s. (1980): "Effects of stimulus intensity on P300" Progress in brain research, 54, 296-300.

Roth, W.T., Blowers,G.H., Deyle, C.M., and Kopell, B.s.(l982): "auditory stimulus intensity effects on components of the late positive complex". Electroenceph. Clin.Neurophysiol, 54, 132-146.

Rot&, W.T., Dorato, K.H., and Kopell, B.s. (1984): "Intensity and task effects on evoked physiological responses to noise bursts". Psychophysiology 21, 466-481.

Ruchkin, D.S., Sutton, S., and Stega, M. (1980b): "Emitted P300 and slow wave event related potentials in guessing and detection tasks". Electroenceph. Clin.Neurophysiol. 80, 35-47.

Rugg, M.D. (1984a): "ERP in phonological matching tasks". Brain and Language, 23, 225-240.

Rugg, M.D. (1984a): "Event related potentials and phonological , . processing of words and non-words". Neuro-Psycholoqica, 22, 435-443.

Rugg, M.D., (1985a): "Effects of handedness on event related potentials in a rhyme matching task". Neuro-psychol. 23, 765-775.

Satterfield,J.H., schell, A.M., Backs, R.W., and Hidak, K.C. (1984): "A cross sectional and longitudinal study of age effects of electrophysiological measures in Hyperactive and normal children". Biol. Psychiat. 19,973-990.

Satterfleld, J.H., schell, A.M., and Backs, R.W. (1987): "Longitudinal study of AERP in hyperactive and normal children: Relationship to antisocial behaviour". Biol, Psychiat, 22, 531-536.

Sklare, D.A., and Lynn, G.E. (1984): "Latency of the P3 event related potential: normative aspects and within subject variability". Electroenceph. Clin.Neurophysiol. 59, 420-424.

Smith, D.B.D., Donchin, E,, Cohen, L., and Starr, A. (1970): "Auditory averaged evoked potentials in man during selective binaural listening". Electro-enceph.Clin.Neurophysiol. 28,146-152.

Smith, D.B.D., Michelewski, H.J., Brent, G.A., and Thompson, L.W. (1980): "Auditory averaged evoked potentials and aging: Factors of stimulus, task and topography". Biological Psychology, 11, 135-151.

Spongberg, T..pecker, T.N. (1990): "Auditory P3 latency and amplitude relation to earlier exogenous auditory events"., Scan.Aud. 19, 73.

Snyder, E., Hillyard, S., and Galambos, R. (1980): "similarities and differences among the P3 waves to detected signals in three modalities" Psychophysiology, 17, 112-122.

Squires, K.C., Hillyard, S.A., and Lindsay, P.H. (1973a): "Cortical potentials evoked by confirming and disconfirming feedback following an auditory discrimination". Perception Psychophys.l3, 25-31.

Squires, N.K., Squires, K.C., and Hillyard, S.A. (1975): "Two varieties of long latency positive waves evoked by unpredictable auditory stimuli in man". Blectroenceph. Clin.Neuro-Pbysiol. 38, 387-401.

Squires,K.C., HalRyard, S.A., and Lindsay, P.H. (1973b): "Vertex potentials evoked during auditory signal detection: Relation to decision criteria". Perception Psychophys. 14, 265-272.

Squires, N.K., Donchin, E., and Squires, K.c. (1977): "Bisensory stimulation inferring decision related processes from P300 component". J.Exp.Psychol. Hum.Percept.Perf. 3, 299-315.

Squires, K.C., Chippendale, T.J., Wrege, K.S., Goodin, D.s. and Starr, A.(1980): "Electrophysiological assessment of mental function in aging and dementia" In L.Roon (Ed.) Aging in the 1980s Psychological issues. America^ Psychological Association, Washington, D.C. 125-134.

Squires,K.c., Hecox, K.c. (1983):" Electrophysiological evaluation of higher level auditory processing" Semin.Hear, 4, 415-433.

Sutton, S.P., Tueting,J., Zubin, and E.R.John (1967): "Information delivery and the sensory evoked potential". Science, 155, 1436-1439.

Sutton, S.P., Braren, M., zubin, J., and John, E.R.(1965): "Evoked potential correlates of stimulus uncertainty", science, 150, 1187-1188.

Sutton, S.P. (1971): "The sensitivity of the evoked potential to psychological variables". Electroenceph.Clin.Neurophysiol. 31, 3O2(A71

Sutton, S.P. (1979): "P300-thirteen years later". In. H. Begleited (Ed).Evoked Brain Potentials and Behaviour, Plenum Press, New York, 107-126.

Syndulko,K., Hansch, E.C., Cohen, S.N. (1982): "Evoked potentials in the assessment of brain function in Senile dementia". In CouBjon, J., Muguiere, F., Revol.M.(Eds). Advances in Neurology: Clinical applications of evoked potentials in neurology, Vol.32, New York, Raven Press, 279-85.

Tyler, L.K. (1985): "The structure of the initial cohort evidence from gating". Perception and Psychophysics, 33, 417-427.

Wada, S., and Starr, R. (1983): "Generator of ABR III effects of lesions of the SOC LL and inferior colliculus on the ABR in the guinea pig". EEe. Clin.Neurophvsiol. 56, 352-366.

Wilkinson, R.T., and Lee, M.v. (1972): "Auditory evoked potentials and selective attention"Blectroenceph. Clin.Neurophysiol. 33, 411-418.

Wood, et al. (1980, 1983): Cited in "The hoppocampal formation as a source of the slow endogenous potentials", Okada, Y.G., Kaufman, L. and Williamson, S.J. (Ed.). Electroenceph.Clin.Neurophysiol, 55, 417-426.

Wood, C.C., and Wolpan, J.R. (1982): "Scalp distribution of human auditory evoked potentials. II.Evidence for overlapping sources and involvement of auditory cortex". Electroenceph.Clin.Neurophvsiol. 54, 25-38.

Woodward, S.H., Owens, J., and Thompson, L.W. (1990): "Ward to word variation in event related potentials component latencies spoken words". Brain and Language, 38, 488-503.