

Human Information Processing During Sleep:
The Late Auditory Evoked Potentials

by

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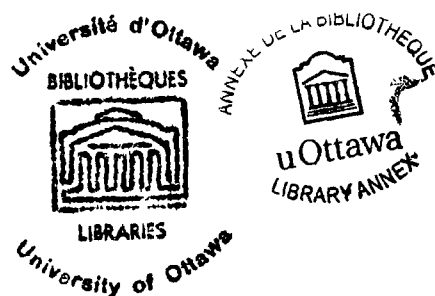
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Abstract

Late auditory evoked potentials were examined during natural sleep. Exogenous components are apparently unaltered by sleep. By comparison, endogenous components are markedly altered. The purpose of the present thesis was to examine the exogenous-endogenous nature of two evoked potential wave forms: the N1-P2 complex and the mismatch negativity (MMN). Two different experiments were run. In the first experiment, the evoked potential wave form was recorded to a train of auditory stimuli. The intensity (50 vs 80 dB SPL) and rate of presentation (1100 vs 3300 msec) of binaurally presented stimuli was varied. In addition, stimuli were monaurally presented in separate runs to the left and right ears. Subjects were tested in the evening while they were reading, and during sleep in stages 2, 3, 4 and REM. The amplitude of P1 and P2 increased in sleep relative to wakefulness whereas the amplitude of the N1 components (N1a, N1b, N1c) were significantly reduced in sleep. These changes appeared to be due to the removal of a large, slow negative component ("wNd") in the sleep wave forms. The wNd overlapped the P1, N1 and P2 components during wakefulness. The P1 and P2 were generally found to vary as a function of the experimental manipulations and were therefore suggested to reflect exogenous processes. N1a, b and c were very much attenuated in non-REM sleep, often falling below baseline. As such, a radical interpretation of the N1 complex might be that it is largely, if not entirely,

endogenous in nature in the waking subject.

The second experiment examined the MMN. It has been suggested that it is an exogenous component that occurs independently of the subject's level of attention when a "deviant" stimulus is presented among a train of regularly occurring "standards". As such, the MMN should be invariant in the sleeping subject. In the present study, both deviant probability and the degree of standard-deviant frequency mismatch were varied. Stimulus probability was varied with deviant (2000 Hz) and standard (1000 Hz) stimuli being presented at probabilities of .20 and .80 in a first condition, and .40 and .60 in a second condition. In the frequency mismatch manipulation, deviant stimuli ($p=.20$) were presented in separate conditions at a frequency of 2000, 1250 or 1050 Hz while the standard stimulus ($p=.80$) was maintained at a constant 1000 Hz. Subjects were tested in the evening while they were awake and either attending to the auditory stimuli (counting the deviants) or ignoring them (reading a book). They were then tested in stages 2, 3, 4 and REM of sleep. A larger MMN was generally seen in the reading than in the counting condition in the waking subject. In sleep, the MMN could not be identified in either stage 2 or slow wave sleep occurring within the first half of the night. Possible MMNs were however observed in stage 2 and REM in the second half of the night. In the low frequency separation condition, the negativity in sleep fulfilled the criteria established for the definition of the MMN. In other conditions, the apparent MMN was not always significantly above baseline and its onset was unusually

early. Its scalp topography however was consistent with that of MMNs recorded previously. Although the data were not conclusive, it does appear that a reliable MMN can be observed in sleep. This therefore supports the notion that it is largely exogenous in nature.

Acknowledgements

This thesis represents the culmination of several years work. I have been fortunate to have completed it under the experienced guidance of Dr. Kenneth B. Campbell. He has been patient and understanding throughout this time and has helped to make my studies both satisfying and rewarding. I have come to share his dedication and enthusiasm for research. For these things and more I will always be grateful. Thank you Ken!

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My parents deserve special recognition. They accepted without complaint the time I spent away from them working late and long hours in the laboratory. They thought only of my interests and were always ready to provide what ever support they could. I cannot thank them enough for their patience and support.

Curriculum Studiorum

Ian Bell was born in Ottawa on the 28th day of August, 1958. He completed a B.A. in Psychology at the University of Ottawa in the spring of 1982. In his final year as an undergraduate, he played intramural hockey on a team which did not score a single goal in the first three months of their schedule. The goal keeper for the team was none other than Dr. Kenneth Campbell. Ian's decision to work as a doctoral student under the supervision of Dr. Kenneth B. Campbell was, to a small extent, based on a desire to help reduce Ken's goals-against-average by playing defence. But more importantly, Dr. Campbell's expertise in such areas as computers, statistics, methodology had made him a formidable and respected researcher in the field of Evoked Potentials.

PUBLICATIONS

Bell, I. and Campbell, K.B. and Deacon-Elliott, D. A peak detector program for Event-Related Potentials. (submitted to the International Journal of Psychophysiology).

Campbell, K.B., McGarry, P.A. and Bell, I. Information processing during sleep: the effects of high stimulus intensity. In: W.P. Koella (Ed), Sleep '86, Gustav Fischer Verlag, Stuttgart, 1986, in press.

Deacon-Elliott, D., Bell, I. and Campbell, K.B. Estimation of auditory thresholds during sleep using brainstem auditory evoked potentials (BAEP). (submitted).

Stuss, D.T., Ely, P., Hugenholtz, H., Richard, M.T., Larochell, S., Poirier, C.A. and Bell, I. Subtle neuropsychological deficits in patients with good recovery after closed head injury. Neurosurgery, 1985, 17(1), 41-47.

ABSTRACTS AND CONFERENCE PROCEEDINGS

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Campbell, K.B., Bell, I. and Deacon-Elliott, D. Stimulus-related influences of the evoked K-Complex. In W. Koella (Ed.), Sleep, 1984, Proceedings of European Sleep Congress, Munich, Frg, 1984.

Campbell, K.B., Makasare, M., Bell, I. and Stelmack, R.M. A microcomputer system for the evoked potential laboratory. Psychophysiology, 1985, 5:586.

Deacon-Elliott, D., Bell, I. and Campbell, K.B. Auditory thresholds as measured by brainstem evoked potentials during sleep.

Sleep Research, 1984, Proceedings of APSS, Toronto, 1984.

Deacon-Elliott, D., Campbell, K.B., Suffield, B.S. and Bell, I.

Speed-accuracy tradeoff in closed head-injured outpatients. Paper presented at the International Congress of Electroencephalograph and Clinical Neurophysiology, 1985.

Suffield, B., Campbell, K.B. and Bell, I. Contingent negative variation (CNV) measures of under- and over- processing after severe closed head injury. A paper presented at the 1986 meeting of the International Neuropsychological Society.

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Organizational Note

The text of this dissertation consists of three chapters. The Tables, Figure Legends and Figures referred to within each chapter are placed at the end of the end of the corresponding chapter. These materials are numbered in accordance with the chapter such that, for example, Table 1.1 is the first Figure in the first chapter. All references are presented before Appendix A at the end of the dissertation.

Chapter 1

Introduction

Scalp recordings of the human auditory evoked potentials (AEP) can be used to study the electrophysiology manifestations of sensory or psychological processing in the nervous system. The scalp electrodes record the net electrical change (the "evoked potential") elicited in the nervous system by sensory stimulation or psychological events. The evoked potential may represent electrical activity from one or more generator processes. The activity from these sources will summate both temporally and spatially and will be manifested as negative and positive deflections (or "components") in the evoked potential wave form. A major objective of this type of research is thus to isolate and explain the underlying sensory and/or cognitive processes reflected in the components of the evoked potential.

Components of the Auditory Evoked Potential

The auditory evoked potential wave form consists of a series of positive and negative peak components (Picton, Hillyard, Krausz and Galambos, 1974). These components appear within characteristic time intervals and are often classified according to their peak latency as being early (1-12 msec), middle (12-50 msec) and late (50-800 msec) (Davis, 1976). These responses have also been classified according to the extent to which they are effected by physical characteristics and/or informational content of the eliciting

stimulus (Donchin, Ritter and McCallum, 1978). Evoked potentials that vary as a function of the physical characteristics of the stimulus are labelled as "exogenous" components. For example, manipulation of the physical intensity, frequency or rate of presentation of the stimulus has a marked effect on the exogenous components of the evoked potential. The early and middle latency responses typically fall within this classification. On the other hand, the response characteristics of an evoked potential may reflect the psychological state of attentiveness of the subject or the informational content of the eliciting stimulus. Such a component is labelled "endogenous". Several of the late AEP components reflect largely endogenous processes. Physical manipulation of the stimulus has minimal effect on these components.

The first study in this thesis is primarily concerned with the late components of the AEP often labelled as "P1", "N1" and "P2" (Picton et al., 1974) and a still later negative deflection referred to as the "basic N2" (Naatanen, in press). Stimuli in other modalities may elicit similar P1, N1, P2 components although there may be variation in morphology and/or scalp topography (Davis, Osterhammel, Wier and Gjerdingen, 1972; Goff, Matsumiya, Allison and Goff, 1977). P1 appears as a positive deflection in the AEP wave form that peaks about 50 msec after stimulus onset. It appears to be maximum over the central areas of the scalp (Goff et al, 1977). The frequently studied N1-P2 complex consists of a large negative deflection (N1) peaking at about 100 msec followed by a large positive deflection (P2) peaking at about 175 msec (Davis, 1976).

N1 and P2 show a fronto-central distribution with N1 being more frontally distributed than P2 (Simson, Vaughan and Ritter, 1976, 1977). Because the P1-N2-P2 complex is large over the central or vertex portion of the scalp, it has often been called the "vertex potential". When stimuli are presented monaurally to the left or right ear, additional N1 deflections may be seen at temporal locations. These additional components peak slightly earlier (75 msec) and later (130 msec) than the vertex N1. The earlier temporal component has been referred to as "N1a" whereas the later has been referred to as "N1c" (McCallum and Curry, 1980) the vertex N1 thus becoming "N1b". At about 250 to 300 msec after stimulus onset the 'basic' N2 appears as a slight negative deflection.

When an experimental design employs two or more stimuli, additional components can be elicited in the AEP wave form depending on the demands made of the subject. In the "odd ball" paradigm, subjects must detect infrequent "target" stimuli that are randomly presented among a train of more frequently occurring "standards". The standard and target stimuli can differ along one of many dimensions - intensity, frequency or duration having been often employed. Conscious, effortful processing is reflected in the AEP wave form in a number of different ways. The most salient feature in wave forms elicited by the 'target' stimuli are late N2 and P3 deflections (Sutton, Tueting, Zubin and John, 1967; Ford, Roth and Kopell, 1976; Squires, Donchin, Herning and McCarthy, 1977; Simson et al., 1977; Donchin et al., 1978; Hillyard and Picton, 1979; Ritter, Simson, Vaughan and Friedman, 1979). During auditory

discrimination tasks, the target N2 has a fronto-central distribution similar to the basic N2 elicited in the single stimulus design (Simson et al., 1977). While N2 displays many characteristics of an endogenous component, it is nevertheless modality specific. For example Simson et al. (1977) noted that the target N2 in the visual modality displayed a parietal-occipital distribution whereas that in the auditory modality was maximally distributed over fronto-central areas of the scalp. The peak latency of the target N2 is much more variable than the basic N2 seen in single stimulus designs. Increasing the difficulty of discriminating the target from standard results in an increase in N2 latency. There is some controversy surrounding the effects of the difficulty of target detection on N2 amplitude. Some (Naatanen, Hukkanen and Jarvilehto, 1980b) report that N2 amplitude decreased with increasing difficulty whereas others report no changes (Ford et al., 1976; Perrault and Picton, 1984b) or increases in amplitude (Fitzgerald and Picton, 1983). Perrault and Picton (1984b) suggested these differences might be attributed to "different degrees of attentional engagement in the discrimination task" (p.273). The target-evoked N2 is generally elicited in association with a large parietal-maximum positivity referred to as "P3" or "P300" (Pritchard, 1981). Unlike N2, the scalp distribution of P3 is independent of stimulus modality (Simson et al., 1977). Indeed it can be elicited when subjects are asked to detect the occasional omission of a stimulus presented in a train of regularly occurring stimuli. Since P3 appears to be largely independent of the physical

stimulus per se, it is classified as an endogenous evoked potential.

The peak latency of P3 is quite variable (280 to 500 msec) and is determined by the task demands employed in an experimental paradigm similar in many ways to N2 latency. In simple stimulus discrimination tasks, P3 is characteristically recorded at about 300 msec after stimulus onset (hence the alternate nomenclature "P300").

P3 has been interpreted as a measure reflecting conscious processing of the informational significance of a stimulus (Campbell, Courchesne, Picton and Squires, 1979; Duncan-Johnson and Donchin, 1982). P3 varies inversely in amplitude with the probability of occurrence of the target. Because of its relationship to stimulus expectation and because P3 often occurs after the subject's actual behavioural response (for example, a button press) Donchin et al. (1978) has suggested that P3 reflects a "contextual updating" process. When subjects are asked to ignore all stimuli, the N2-P3 complex will rarely be elicited. Naatanen, Gaillard and Mantysalo (1978, 1980a) suggested the ignored target stimuli nevertheless elicits a negativity at about the time of N2. They called this early N2 the "Mismatch Negativity". This component will be described in more detail in a later section

The Vertex (N1-P2) Potential

Since the advent of signal averaging (Dawson, 1954), N1 and P2 have long been a focus of inquiry in evoked potential research. They can be elicited in simple experimental designs using a train of repetitive stimuli. Just as the early and middle latency responses have been shown to be sensitive to changes in the physical qualities

of the stimulus, so too the vertex N1 and P2 components vary as a function of stimulus parameters such as their intensity, frequency and rate of presentation. Decreasing the rate of stimulus presentation produces an increase in N1 and P2 amplitude (Davis, Mast, Yoshie and Zerlin, 1966; Nelson and Lassman, 1968; Picton, Woods, Baribeau-Braun and Healy, 1978). Davis and Zerlin (1966) indicated the refractory period of N1-P2 was perhaps as long as 10 sec. Increases in stimulus intensity will also produce an increase in N1-P2 amplitude (Davis and Zerlin, 1966; Picton, Goodman and Bryce, 1970; Picton et al., 1978).

As may be expected from exogenous evoked potentials, N1 and P2 are modality specific components in that their scalp topography varies with the modality of sensory processing. The auditory modality N1 and P2 have a fronto-central distribution with P2 being distributed somewhat more posteriorly to N1 (Simson et al., 1976, 1977). In the somatosensory modality, the N1- and P2-like wave forms are prolonged in latency (as might be expected given the length of the sensory pathway) and have a more central distribution (Goff et al., 1977). N1, in the visual modality, is maximum in the occipital region whereas P2 has a parietal-central distribution (Simson et al., 1976, 1977).

Nonsensory endogenous factors, especially the subject's level of attention, have also been reported to alter N1 amplitude. In a now classic, study Hillyard, Hink, Schwent and Picton (1973) provided strong evidence to show that the distribution of selective attention among multiple stimulus channels could be reflected in the

evoked potential wave form. The effect was reported as a change in N1 amplitude. In many previous studies, subjects were asked to attend to one task and ignore another. The problem with these studies was that in many cases stimuli were presented in a non-random, predictable manner (for reviews see Karlin, 1970; Naatanen, 1975). Alterations in N1 amplitude could therefore be explained by a change in non-selective preparatory state rather than selective attention per se. On the other hand, studies that employed random sequences of stimuli often used slow rates of presentation. Usually no effect of attention was found on N1-P2 with such long ISIs. It was possible for subjects to attend to one "channel" and then switch to the "ignored" channel thereby maximizing information input even though instructions may have been otherwise. Hillyard et al. (1973) controlled for these problems by implementing several key features into their design. A brief description of their research will be presented.

In a first experiment, subjects were instructed to attend to a series of tone pips in a designated ear ("relevant" stimuli) while ignoring a concurrent series delivered to the other ear ("irrelevant" stimuli). The series in the right and left ears were presented independently of one another. It was therefore possible for stimuli to be simultaneously presented in both ears. One of the stimuli presented in each ear (or "channel") was presented at a higher probability (the "standard" stimulus) than a second stimulus (the "target") in that series. Standard tone pips of 800 Hz and 1500 Hz were delivered to the left and right ears respectively at a

random ISI ranging from 250 to 1250 msec. Approximately 10% of the left ear stimuli were targets presented at a frequency of 840 Hz while 10% of the right ear stimuli were targets presented at a frequency of 1560 Hz. Subjects were asked to count the number of targets occurring in a designated ear. Verification of the count provided behavioural evidence that the subject was actually attending to the designated ear. An important feature in their design was the left ear stimuli were clearly distinguishable from the right ear stimuli making it relatively easy for subjects to attend to one of the channels and ignore the other. Moreover, the standard-target frequency separation was so small that subjects necessarily had to be attentive to the designated channel to successfully make the discrimination. The demands of such a task thus made it unlikely that subjects were able to attend both ears with equal efficiency (i.e: the cost of switching from one ear to another would be an increase in the number of misses). The effect of selective attention was reported as an enhanced N1 to attended stimuli relative to unattended stimuli. Hillyard et al. (1973) conducted a second study to ensure this effect was not due to "rapid fluctuations of some nonselective preparatory state that might have become partially locked to the schedule of tones in the attended ear. If such hypothetical changes in state increased all evoked potentials nonselectively, those in the attended ear would be preferentially enhanced because its stimulus schedule would be more closely coupled to the cycles of the preparatory state" (p.179). Instead of presenting the series of stimuli in the left ear

independently of the series in the right ear, all stimuli were presented in a single temporal sequence. The results were essentially the same although the increase in N1 amplitude in attend condition relative to ignore conditions was not as large as in the first study. This attentional effect suggested that N1 could be characterized, not only as reflecting exogenous processes, but also an endogenous process. Due to its dual nature, N1 has been referred to as a "mesogenous" evoked potential.

A number of additional studies were conducted in order to determine the conditions under which the "N1" effect was best elicited (Schwent, Hillyard and Galambos, 1976a,b; Schwent, Snyder and Hillyard, 1976c; Parasuraman, 1978). These series of studies concluded that for N1 to differ between attended and ignored channels, stimuli had to be presented at fast rates and the intensity of competing unattended stimuli had to be kept relatively low. When stimuli were presented at slow rates (greater than 800 msec) or at high intensities, the N1 effect was not produced. It appeared that in these conditions, subjects were unable to ignore the unattended, competing channel.

Naatanen et al. (1978) later suggested an alternative explanation of the N1 effect. In studies in which N1 was shown to vary with manipulations of selective attention, the effect appeared to begin prior to the actual N1 peak and last for some time following it. A slow negative wave therefore appeared to overlap N1, summing to it and P2. In contrast to the random ISI paradigms employed by the Hillyard and his colleagues, Naatanen et al. (1978,

1980a) presented stimuli at a slow, constant ISI of 800 msec. Consistent with the Schwent et al. studies, they did not find that N1 amplitude was enhanced to attended stimuli. Nevertheless, during the downslope of N1, the wave forms to attended stimuli became more negative relative to wave forms elicited by the same stimuli when they were not attended. This negativity continued for several hundred milliseconds. This difference between attend and ignore wave forms was labelled the "Processing Negativity" since the negative shift was thought to reflect differential processing to attended stimuli. The Processing Negativity is best seen in the "difference" wave form obtained by subtracting unattended from the attended wave forms.

An extensive investigation of the Processing Negativity has subsequently replicated the results of Naatanen et al. (1978) and shed some insight into the nature of this attentional-related component (see reviews by Naatanen and Michie, 1979; Naatanen, 1982). Hillyard's own laboratory has also identified a long-lasting overlapping negative wave labelling it "Nd" to refer to the difference in negativity due to increases in the subjects level of attention (Hansen and Hillyard, 1980). The rather vague "Nd" label, in contrast to Naatanen's "Processing Negativity", was chosen to avoid attaching a functional significance to the wave form. The Processing Negativity (or "Nd") has been reported to consist of a shorter latency central component (peak latency of 150 to 200 msec) and a later frontal component (peak latency of 300 to 400 msec) (Hansen and Hillyard, 1980; Naatanen, Gaillard and Varey, 1981).

The onset of the Processing Negativity has been shown to vary as a function of the ISI (Parasuraman, 1980; Naatanen et al., 1981; Hansen and Hillyard, 1984) and the ease with which relevant stimuli can be distinguished from irrelevant stimuli (Hansen and Hillyard, 1980, 1983; Okita, 1981). The process of identifying relevant stimuli (to be attended) from irrelevant stimuli (to be ignored) is speeded with increasing rates of stimulus presentation. In such instances, the onset latency of the Processing Negativity decreases as the ISI is shortened. With sufficiently short ISIs, the Processing Negativity will overlap with N1 and P2 as was evident in Hillyard and his colleague's early studies. The effect in the evoked potential wave form is therefore seen as a negative enhancement of N1 but a diminution of P2 amplitudes to attended stimuli relative to when they are ignored. With sufficiently long ISIs, the subject has ample time to discriminate the irrelevant from the relevant stimuli. The onset of the Processing Negativity is delayed such that it is temporally dissociated from the exogenous N1-P2 complex (Naatanen et al., 1978, 1980a, 1981; Parasuraman, 1980). As such, there is no difference between the N1 amplitudes in the relevant and irrelevant channels. Previous failures to find an enhanced N1 to attended channels when slow rates of presentation were employed (Schwent et al., 1976b) could thus be attributed to later onset of the Processing Negativity. The onset of the Processing Negativity also varies according to the ease or difficulty with which the relevant stimuli can be discriminated from the irrelevant stimuli. Hansen and Hillyard (1980) varied the

frequency separating relevant from irrelevant channels by 50, 100 and 400 Hz. The onset of Nd was delayed and its amplitude was reduced as the difficulty of discrimination (decreasing frequency separation) was increased. Alho, Sams, Paavilainen and Naatanen (1986), on the other hand, failed to replicate these findings. As they acknowledged, the differences in pitch separations between their experimental conditions (20 to 167 Hz) were much narrower than Hansen and Hillyard's (1980) and thus was probably not large enough to produce a latency shift.

Naatanen (1982) has hypothesized that the early central component of the Processing Negativity reflects a gradual process of matching the physical attributes (features) of sensory input with a neuronal trace of the attended stimulus channel. This neuronal representation is referred to as an 'attentional trace'. All stimuli, whether relevant or irrelevant are compared to the hypothesized trace. This involves a feature-by-feature comparison of the stimulus with the trace which only terminates when a mismatch occurs or all attributes are successfully matched in a discrimination task. A partial Processing Negativity will therefore be elicited by all stimuli in a dichotic listening task. The comparison process will be abruptly terminated to stimuli that differ significantly from the attentional trace. On the other hand, when the sensory input closely resembles the trace a more extensive analysis is required and hence the Processing Negativity will be quite pronounced. The attentional trace was suggested to be a temporary neuronal representation which is maintained by conscious rehearsal

of a "vivid perception-kind of mental image of the attended stimulus" (p.629) and continued afferent input from the attended stimulus channel. This hypothesis implies that in reading conditions when subjects are instructed to ignore the auditory stimuli, a mental image of the auditory stimuli (the attentional trace) will not be formed. As a consequence, the Processing Negativity should not be elicited to auditory stimuli when subjects are not actively attentive (e.g. they are reading) to them (Naatanen, see note 1).

Since the attentional enhancement of N1 has largely been attributed to the Processing Negativity, the mesogenous nature of N1 itself can be questioned. N1 has been described as an exogenous evoked potential since, as already mentioned, it is affected by manipulations of quality of the physical stimulus. However, there is an alternative explanation of this apparent exogenous effect. Manipulations of the physical stimulus may also alter the subject's level of attention. For example, it may be impossible to ignore a very loud stimulus or one that is presented infrequently even if the subject is asked to do so. Thus increases in N1 amplitude with either increasing stimulus intensity or long ISIs may be due to changes in the actual physical nature of the stimulus or a possible change in the level of attention of the subject. In a recent study, Perrault and Picton (1984a) noted that N1 amplitude to a 90 dB SPL tone pip presented 1/1.1 sec was identical when the subject was engaged in an auditory frequency discrimination task or when they were asked to ignore the auditory stimuli and read a book. It could

be argued that N1 in the ignore condition is a manifestation of its exogenous characteristics. Equally, it could be argued that N1 was at least partially endogenous since subjects are unable to ignore such loud stimuli. The dilemma for the evoked potential research is how can the exogenous portion of the vertex potential be distinguished from a possible endogenous portion. In a recent study, Alho et al. (1986) concluded that "since even to-be-ignored stimuli elicit some Processing Negativity, the difference wave obtained by subtracting the ERP [event-related potential] to these stimuli from the ERP to the same stimuli when they are to be attended does not, of course, yield the whole Processing Negativity.

This is because the common part [i.e. the portion due to the attentional process] is cancelled out in the subtraction procedure and, consequently, the difference wave should be called the processing-negativity difference rather than the Processing Negativity" (p.196). To dissociate exogenous from endogenous effects would require the subject to be totally unaware ("inattentive") of the evoking stimulus. In the conscious, awake subject, this is probably not possible. On the other hand, the period in which the subject is least likely to be conscious of external stimuli is when they are asleep. Rather surprisingly, while evoked potentials have been recorded in sleep results have not been consistent.

Evoked Potentials During Sleep

The effects of natural sleep have been examined for the early, middle and late auditory evoked potentials. Tables 1.1, 1.2 and 1.3

presents a summary of these studies. Apart from the early "brainstem" evoked potential, there have been few consistent findings. As is apparent in these tables, a variety of methodological problems make definitive conclusions difficult. Sample size in many sleep studies is small. Because of the small sample sizes the statistical power to reject the null hypothesis (of a difference between waking and sleeping waveforms) is often poor. In many studies, constancy of stimulus input to the ear cannot be assured. Typically, free-field loudspeakers mounted at a fixed distance above or beside the subject have been employed to transduce the auditory stimulus. Slight changes in head position or body movement within sleep will markedly distort the characteristics of stimulus input and hence the morphology of the evoked potential. The use of ear insert speakers affords greater control of input. In general, however, such speakers are not easily calibrated. Moreover, because human ears vary considerably in size, even ear insert speakers may change position during the night.

----- Insert Table 1.1, 1.2 and 1.3 here -----

The evoked potentials recorded in sleep have been measured in different ways. Peak-to-peak measurement is common. Peak-to-peak measurement is dependent on the amplitude of two components of the evoked potential. Hence a change in peak-to-peak amplitude could be due to a change in either or both components. When components (such as N1 and P2) are overlapped by slow waves such as the Processing

Negativity, matters are even more ambiguous. As noted, N1 may increase and P2 may decrease in amplitude with manipulation of selective attention, the N1-P2 peak-to-peak measure therefore showing no alteration. Hence, it is entirely possible that peak-to-peak measurement may completely mask an experimental effect. Ideally, a baseline-to-peak measure should be employed. The average amplitude in the pre-stimulus interval usually serves as a baseline from which peak deflections are measured. In the absence of a pre-stimulus period, some authors employ the amplitude of the evoked potential at stimulus onset as a pseudo-baseline. This is however subject to distortion by stimulus artifact. Finally, there has been little inter-laboratory consistency with respect to stimulus parameters. Some laboratories employ click stimuli, while others use tone pips of varying frequency and duration. Stimulus intensity and rate of presentation rarely controlled. Generalization across studies is therefore difficult.

The Early Components

As may be observed in Table 1.1, there is agreement that sleep and level of attention have little effect on the early components (first 10 msec) of the auditory evoked potential (Amadeo and Shagass, 1973; Osterhammel, Shallop and Terkil_udsen, 1985; Erwin and Buchwald, 1986). This is the case even when stimuli are of very low (Deacon-Elliott, Bell and Campbell, 1986) or high intensity (Campbell and Bartoli, 1985) and regardless of their rate of presentation (Campbell and Bartoli, 1985).

The Middle Components

The data on the effects of sleep on the middle components are much less consistent (Table 1.2). Mendel and Goldstein (1969) initially found the middle latency responses (MLR) remained constant in subjects tested in sleep. In a later series of studies, they reported the amplitude of Na-Pa was smaller in sleep than in wakefulness with larger decreases occurring in stage 3 and 4 than in stages 2 and REM (Mendel and Goldstein, 1971a, 1971b). Their latencies did not vary with level of arousal. However, Mendel and Kupperman (1974) found the latency of Pa and Nb were slightly shorter in REM (rapid eye movement) than in non-REM sleep. No differences in amplitude were found in this study. Mendel (1974) indicated that both the latency and amplitude of the MLR were constant in sleep. In a more recent study, Osterhammel et al. (1985) reported that differences between wakefulness and sleep could first be seen at about the latency of Pa. The Nb and Pb (Pb corresponded in time with P1) components were delayed in sleep with the delay being greater in stages 3 and 4 than in stages 1 and 2. The amplitude of Pa-Nb was also smaller in sleep than wakefulness. Their figures also suggested Nb-Pb was reduced in sleep although they did not make specific reference to this component. Erwin and Buchwald (1986) have replicated these findings. They reported the complete disappearance of Nb within non-REM (NREM) sleep although it returned to near waking levels in REM sleep.

The Late Components

Table 1.3 summarizes the effects of sleep on the late components of the AEP. Studies of the late auditory evoked

potentials in the sleeping subject have labelled peak deflections according to the conventional nomenclature applied to waveforms recorded during wakefulness. It is doubtful that the same components are being measured. For example, a long latency, large amplitude, fronto-central component labelled as "N2-P3" within sleep is probably part of the K-Complex. It is certainly different from the endogenous N2-P3 seen in the waking subject. Moreover, the N2-like wave that appears to increase as subjects become increasingly drowsy is probably different from the N2-like wave that forms part of the K-Complex. Ujszaszi and Halesz (1986) have recently noted that the early (300 msec latency) "N2a" has a central distribution while the later "N2b" (500 msec latency) takes on a prefrontal-frontal distribution confirming Campbell, Bell and Deacon-Elliott's (1985) earlier findings. They therefore have different intra-cranial generators and probably reflect different functional properties.

There are conflicting reports as to how changes in level of arousal affect P1 amplitude. When measured relative to a pseudo-baseline, P1 has been reported to increase in amplitude as subjects shift from wakefulness to drowsiness to sleep (Weitzman and Kremen, 1965; Williams, Tepas and Morlock, 1962; Williams, Morlock, Morlock and Lubin, 1964) or remain more or less constant in amplitude (Fruhstorfer and Bergstrom, 1969). The figures in these studies indicate P1 was slightly larger during the non-REM stages of sleep than during REM sleep. On the other hand, Anch (1977) and Kevanishvili and Specht (1979) found P1-N1 amplitude was smaller

during sleep than during wakefulness. In the former study, P1-N1 was smallest during REM sleep and only slightly larger during sleep stages 2, 3 and 4. In the latter study, the peak-to-peak P1-N1 was smaller in stages 3 and 4 than stage 2 and REM. The amplitude during REM sleep was approximately equal to that seen in stage 2. Such changes could however be due to manipulations in N1 rather than P1. Erwin and Buchwald (1986) measured P1 amplitude relative to a baseline established at stimulus onset. P1 showed a pronounced decrease in non-REM sleep to the extent that it could not be seen in stages 3 and 4. Its amplitude in REM sleep however approximated that found in wakefulness. Kevanishvili and Specht (1979) found that P1 peaked much later during sleep than wakefulness. They reported P1 latency increased from 61 msec in wakefulness to 108 msec in stage 4. Williams et al. (1962) and Weitzman and Kremen (1965) reported only slight increases in the sleep P1 latency. As already mentioned, the various studies have employed different stimulus parameters, rates of presentation, recording procedures (in particular, filter settings), sample sizes and measuring techniques, any one of which could account for the contradictory findings.

N1 amplitude, whether measured from a baseline or relative to P2, has generally been reported to be smaller in sleep than in wakefulness. The decrease in amplitude from wakefulness to sleep has been found to be as large as from 10 to 20 μ V (Fruhstorfer and Bergstrom, 1969; Kevanishvili and Specht, 1979) or as small as from 1 to 4 μ V (William et al., 1962, 1964; Weitzman and Kremen, 1965)

for both baseline-to-N1 and N1-P2 measures. Williams et al. (1962) reported the average amplitude of N1 decreased from wakefulness sleep stages 1, 2, 3 and 4. N1 amplitude during REM approximated that obtained during stage 2. N1-P2 amplitude in the study by Kevanishvili and Specht (1979) showed substantial decreases from wakefulness to the different sleep stages 1, 2, 3, 4 and REM. In general, most studies have found that N1 peaked at approximately 100 msec during wakefulness and its latency did not vary during sleep. An exception to this rule was reported by Kevanishvili and Specht. N1 latency was found to increase from a low of 110 msec during wakefulness to a high of 165 msec in stage 4 of sleep.

The data for P2 are somewhat more variable than those for N1. Williams et al., (1962, 1964) found P2 underwent a large decrease in amplitude with changes in arousal. It was largest during wakefulness and decreased in amplitude as subjects became drowsy. Further decreases were found as subjects entered the different stages of sleep. Fruhstorfer and Bergstrom (1969) only obtained data for P2 during wakefulness and drowsiness. Their data also suggest that P2 decreases as subjects become less aroused. When P2 amplitude was measured relative to N2 (i.e: P2-N2) it has been found to increase, show no change or decrease in amplitude with sleep onset. Williams et al. (1962) showed P2-N2 was largest during wakefulness and smallest during REM sleep. During non-REM sleep, its amplitude was about the same as that observed in wakefulness. In the Weitzman and Kremen (1965) study, the waking P2-N2 amplitude appeared to equal the sleep P2-N2 in all stages of sleep. The

largest changes in P2-N2 were reported by Kevanishvili and Specht (1979). P2-N2 increased with sleep onset with the largest amplitudes being recorded during stage 2 and stage 3. Its amplitude in stages REM and stage 4 was approximately the same as that in wakefulness. Again, it is difficult to dissociate P2 effects from those of the later N2. As described for the previous P1 and N1 deflections, Kevanishvili and Specht also reported that P2 latency increased with sleep onset. It appeared at least 25 msec later in sleep than in wakefulness (188 msec). While no latency differences were reported by Williams et al. (1962,1964) and Weitzman and Kremen (1965), Fruhstorfer and Bergstrom (1969) found P2 in fact appeared slightly earlier as subjects become more drowsy.

Several studies presented descriptive data for P1, N1 and P2 from single subjects without corresponding statistical analyses. In Fig. 10 of the Picton et al. (1974) article, P1, N1 and P2 appear at slightly later latencies with attenuated amplitudes during stage 2 of sleep. Fig. 3 in the Osterhammel, Davis, Wier and Hirsh (1973) article suggested slight latency shifts for N1 and P2 although no apparent amplitude differences are visible among the waking and light and deep stages of sleep. The effects of stimulus intensity and stage of sleep were however confounded. These results must therefore be considered with caution. In the study by Ornitz, Ritvo, Carr, La Franchi and Walter (1967a), the latencies for P1, N1 and P2 during sleep stages 2 and REM appear to be identical with those observed during wakefulness (their Fig. 1).

Manipulations of stimulus intensity has been carried out in two

studies. Anch (1977) presented tone pips binaurally every second at an intensity of either 50, 65 or 80 dB SPL. Each of his three subjects was tested on 9 separate nights with only one intensity being used per night. The peak-to-peak amplitude of P1-N1 was measured for data recorded during wakefulness, stage 2, slow wave sleep (stages 3 and 4) and stage REM of sleep. Increases in stimulus intensity produced a linear increase in P1-N1 amplitude in both waking and sleep states. At each intensity setting, P1-N1 was largest during wakefulness, intermediate during non-REM sleep, and smallest during REM sleep. Buchsbaum, Gillin and Pfefferbaum (1975) used intensity settings of 50, 60, 70 and 80 dB SPL. Click stimuli were presented at a rate of 1/sec with all intensities being presented in a pseudorandom order within a block of stimuli. Analyses were conducted on a measure they referred to as a "mean deviation". Buchsbaum et al. defined latency windows for components (e.g: P100, N140, P200) that were frequently identified in the waking state. The mean amplitude of data points within a window was subtracted from the amplitude of each data point. The absolute amplitude of these difference values were summed and an average - called the mean deviation - was computed. There was a general tendency for P100, N100 and P200 mean deviations to be largest in stages 3 and 4 but the effect was only significant for the P200 window. Furthermore, stages 3 and 4 were the only periods of sleep during which increases in stimulus intensity were associated with increases in values of the mean deviation. During wakefulness and REM sleep, this measure was larger for the 50 and 70

dB than the 60 and 80 dB intensities.

The most consistent effects of sleep are those reported for the N2 wave form. N2 occurs between 250 to 300 msec during the wakefulness and appears to undergo a progressive increase in latency during sleep: 280 to 320 msec in stages REM and 2; 350 to 370 msec in stages 3 and 4 (Kevanishvili and Specht, 1979; Weitzman and Kremen, 1965). Similar latency values were noted within stage 2 and REM by Ornitz et al. (1967a) and by Osterhammel et al. (1973). Fig. 1 in Williams et al. (1964) appears to indicate an increase in N2 latency with increasing depth of sleep. On the other hand, Fruhstorfer and Bergstrom (1969) reported an opposite effect, with N2 appearing at about 310 msec during waking state and decreasing by as much as 40 msec with sleep onset. Picton et al.'s (1974) example wave forms did not show a latency shift.

The sleep N2 has consistently been found to be larger than the N2 recorded during wakefulness. The increase in N2 amplitude may in fact serve as a index of sleep onset (Ornitz, Ritvo, Everett, Panman and Walter, 1967b; Fruhstorfer and Bergstrom 1969; Noldy-Cullum, McGarry and Campbell, in press). Weitzman and Kremen (1965) suggest N2 is largest during stages 3 and 4 although Kevanishvili and Specht (1979) indicated it is largest in stages 2 and 3. Ornitz et al. (1967b) offer an explanation of this contradiction - N2 appears to be largest soon after sleep onset regardless of the stage of sleep. During REM sleep (typically occurring late at night), N2 amplitude approximated the waking N2. Considerable variations in N2 amplitude may occur during or soon after sleep onset but this appears to

become more stable as sleep progresses (Ornitz et al. 1967a).

During wakefulness, when subjects are asked to detect an infrequently occurring "target" presented at unpredictable intervals among a train of frequently presented "standard" stimuli, a late positive wave, P3, may be observed. It peaks at approximately 300 msec during easy discrimination tasks (see Pritchard, 1981 for a review). A large number of studies have indicated that this parietal maximum component is only elicited when the subject is actively engaged in the sensory discrimination task. When subjects are engaged in a secondary task and are asked to ignore the evoking stimuli, no P3 can be observed (see Donchin, 1981 for a review). Due to the cognitive demands for active attention, it is unlikely the P3 could be observed in the sleeping subjects. This however has not been tested. Recently, Roth and his coworkers (Roth, Blowers and Doyle, 1982; Roth, Dorata and Kopell, 1984; Putnam and Roth, 1986) have reported P3-like wave in the unattentive subject following very loud tones pips presented at slow rates of presentation (greater than 4 sec). Campbell, McGarry and Bell (in press) failed to observe similar P3s in the sleeping subject even when stimulus intensity was quite high (100 dB SPL). They however employed a relatively fast rate of stimulus presentation (every 2.2 sec). There have been reports of late "P3" waves during sleep (Williams et al., 1962; Weitzman and Kremen, 1965; Osterhammel et al., 1973). This P3 is however likely part of the K-Complex. Its latency (800 to 1000 msec) and frontal scalp topography distinguish it from the early (300 msec) parietal P3 seen in signal detection

tasks.

The Temporal N1 Components

There has been a long standing controversy regarding the existence of a vertically oriented dipole in the primary auditory cortex (Peronnet, Giard, Bertrand and Pernier, 1984; Wood and Wolpaw, 1982; Wood, McCarthy, Squires, Vaughan, Woods, and McCallum, 1982; Perrault and Picton, 1984; Scherg and Von Cramon, 1985, 1986) generating the vertex N1. This dipole has been hypothesized to account for differences in EP morphology between temporal and vertex wave forms. A comparison of wave forms at these locations indicates that the temporal evoked potentials consist of additional components, some of which were of opposite polarity to those found in the vertex wave form. Of crucial importance to resolving this issue is whether, in fact, the temporal differences reflect artifact activity introduced by an active reference electrode. Although the controversy has yet to be resolved, it would appear that several components are indeed elicited in the N1 latency range regardless of whether an active (e.g: nose) or an inactive (e.g: sterno-vertebral) reference site is used. Wolpaw and Penry (1975) compared wave forms recorded from Cz, T3 and T4 that were referenced to balanced sterno-vertebral electrodes. Click stimuli were presented to left and right ears with only one ear being stimulated during a run. N1-P2 was elicited at Cz with peak latencies of approximately 100 and 190 msec. At the left and right temporal sites (T3 and T4), the 100 msec negative peak was not seen. Instead two negative peaks were observed. The first peaked slightly earlier than the vertex N1

while the second peaked slightly later. Wolpaw and Penry suggested the temporal wave forms reflected two different processes: a temporal process superimposed on the vertex N1-P2 process. This temporal complex was labelled the "T-complex" and was identified by subtracting the Cz from the T3 and T4 wave forms. The difference wave form consisted of a positive deflection ("Ta") peaking within 100 to 110 msec and a negative deflection ("Tb") peaking within 150 to 160 msec. The negative peaks at temporal sites have also been reported by other researchers (McCallum and Curry, 1980; Perrault and Picton, 1984a; Peronnet et al., 1984; Woods and Wolpaw, 1982). McCallum and Curry (1980) labelled the temporal sub-components, "N1a" and "N1c". The large vertex N1 was therefore labelled "N1b". Such a nomenclature will be used in this thesis. Unless otherwise specified, the general "N1" label will refer exclusively to the vertex N1b.

The functional significance of the temporal N1s remains controversial. McCallum and Curry (1980) claimed N1a was largest in the hemisphere opposite the dominant hand. In right-handed subjects, it was largest in the left hemisphere whereas in left-handed subjects it was largest in the right hemisphere. They did not provide data to support this claim. Their results suggested N1a was not affected by ear of delivery of the stimulus. This was supported by Perrault and Picton (1984a). While McCallum and Curry recorded N1a at an latency earlier than the vertex N1, Perrault and Picton found there were minimal differences in peaks latencies between N1a and N1b. This led Perrault and Picton to suggest N1a

and N1b reflect identical components with the exception that N1a is smaller due to an overlapping positive component (e.g: Ta described by Wolpaw and Penry, 1975). The N1b peak has already been described in an earlier section. N1c has been found to be largest in the hemisphere opposite the ear of stimulation (McCallum and Curry, 1980; Perrault and Picton, 1984a). Perrault and Picton (1984a) reported that N1c was augmented with increases in ISI and was also altered by manipulations of the subject's level of attention to auditory stimuli. Thus N1c, like N1b, appears to reflect both exogenous and endogenous brain processes. Recently Woods and Clayworth (1986) indicated that "Nd" (or the Processing Negativity) can also be observed in temporal sites. The exogenous/endogenous nature of N1c thus remains a subject of debate. If N1a and N1c reflect exogenous processes they should also be observed during sleep.

The Mismatch Negativity

In the often employed "odd-ball" task, infrequent "odd" targets are presented at irregular intervals among a train of "standards". The target differs or deviates from the standard along some stimulus dimension: usually its frequency, intensity or duration. While both target and standard stimuli will elicit similar N1 and P2 components, the target stimuli will also elicit an N2-P3 complex. In a series of studies, Naatanen and his colleagues have noted that such deviant stimuli also elicit an N2 sub-component that they labelled "N2a" or more frequently "Mismatch Negativity" (MMN). Unlike the later N2b-P3 complex, the MMN appears to be elicited regardless of the subject's level of attention. The data obtained

for the MMN have come almost exclusively from studies carried out in this Finnish laboratory. In an early study, Naatanen et al. (1978) conducted two dichotic listening experiments. Stimuli were delivered at random to the left and right ears. Subjects were asked to count the number of target stimuli delivered in a designated ear while ignoring all stimuli delivered to the opposite ear. In the first experiment, standard and target tone pips were presented binaurally. They differed on the basis of their intensity (70 vs 80 dB SPL respectively). In the second experiment stimulus intensity was held constant while their frequency was varied (1000 vs 1140 Hz for the standard and targets respectively). In both experiments, stimuli were delivered at a rate of 1/800 msec. Average wave forms were obtained from Cz, T3 and T4 electrodes. As described in a previous section, the Processing Negativity was seen as a slight negative shift in attended wave forms relative to unattended wave forms recorded to the same stimulus. Target wave forms were also compared to the standard wave forms. An N1-P2 complex was elicited by both target and standard stimuli. Attended target stimuli also elicited a well defined N2 (250 msec)-P3 (300 msec) deflection. Moreover, a large positive deflection (P3) peaking at about 400 msec was elicited by attended targets. Unattended target stimuli also appeared to elicit a positive deflection at about the same latency but of a much smaller magnitude than that to attended targets. The difference between target and standard waves was more readily seen in subtraction wave forms obtained by subtracting the standard from the target wave forms recorded in the same condition. Both attended

and unattended subtraction (difference) wave forms disclosed a slow negative deflection with an onset beginning between 50 to 100 msec and continuing for several hundred milliseconds. Since this slow negativity was elicited regardless of the subjects attentional state, Naatanen et al. suggested the negativity reflected a "mismatch process caused by a sensory input deviating from the memory trace ('template') formed by a frequent 'background' stimulus" (p.324).

N2 may serve as an index of stimulus deviance. It has consistently been reported to be elicited by target stimuli presented within a background series of standard stimuli (Ford et al., 1976; Snyder and Hillyard, 1976; Simson et al., 1977; Naatanen et al., 1980a, 1980b; Naatanen, Simpson and Loveless, 1982; Fitzgerald and Picton, 1983, 1984). Naatanen and his colleagues however suggest N2 is actually composed of two sub-components which frequently cannot be distinguished from one another because of methodological factors (Naatanen and Gaillard, 1983). They proposed that the first component is elicited regardless of whether subjects are attentive or not. It is a response to stimulus deviance or mismatch and was accordingly called the "Mismatch Negativity" (MMN).

The later "N2b" is elicited by deviant stimuli only if they are detected consciously. Within this framework, attended target stimuli elicit both the MMN and N2b components. Ignored target stimuli will only elicit the MMN.

Naatanen and Gaillard (1983) have described the MMN as a ramp-like form since it is characteristically seen as a negative

shift in evoked potentials to target stimuli relative to evoked potentials to standard stimuli. The onset of this shift frequently begins prior to or during the N1-P2 latency range. It has been reported to occur at frontal and temporal electrode sites (Naatanen et al., 1978, 1980a, 1982, 1983) with frontal amplitudes being somewhat smaller than temporal amplitudes (Naatanen et al., 1978, 1980a). This fact suggests it is a modality-specific component. Naatanen et al. (1983) further suggested that the amplitude of the MMN is related to the probability of the target stimuli with lower probability deviants eliciting a larger MMN than higher probability targets.

The nature of the MMN implies the operation of an "automatic" comparative memory process which takes place regardless of the subject's attentional state and/or allocation of conscious effort (Shiffrin and Schneider, 1977; Schneider, Dumais and Shiffrin, 1984). Naatanen (in press) suggests the "standard" regularly occurring stimuli become represented as short duration neuronal traces in the central nervous system. Although all stimuli will be represented by a neuronal trace the strength of a particular trace is determined by the frequency with which a stimulus is presented. Without continued afferent input from the same physical stimulus the trace decays. Hence a trace would only be available for the most frequently and/or recently presented stimuli (Sams, Alho and Naatanen, 1984). Stimuli that are physically different from this trace will elicit the MMN due to "a change in this system of neuronal representations". This hypothesis would then suggest that

in studies employing an odd-ball paradigm, the physical attributes of deviant stimuli are compared with those represented in the neuronal trace of the standard stimuli. When a mismatch occurred, the MMN would automatically be elicited regardless of the subjects level of attention. The MMN is thus elicited by the physical changes in sensory input and as such has been labelled an exogenous component by Naatanen and his colleagues. If the MMN reflects an automatic comparative memory process, it should therefore be apparent even in the unconscious, sleeping subject.

In a recent pilot study, Sams, Paavilainen, Cammann, Alho, Reinikainen and Naatanen (1986) failed to observe an MMN during sleep. Standard 1000 Hz stimuli were presented at a probability of .90. The infrequent stimuli (.10 probability) deviated slightly having tonal frequency of 1050 Hz. In the early portion of the night (stages 2, 3 and 4), the MMN could not be observed. The authors suggested that a greater frequency separation may be required for the functioning of the MMN in sleep. It is also possible that the failure to observe the MMN in the early portion of the night could be due to a low MMN signal-to-noise ratio. The MMN amplitude is quite small (1 to 5 uV) while the background amplitude of delta activity in these stages of sleep can measure several hundred uV. The optimal period for the recording of the MMN may therefore be in the second half of the night during either stages 2 or REM when delta activity is markedly lowered. While REM offers the methodological advantage of a low amplitude background EEG, it is also possible that information processing is quite different in REM

than in non-REM. Brainstem reticular unit activity increases in REM sleep and decreases in non-REM (Steriade, Oakson and Ropert, 1982). Many studies have indicated that waking thresholds are lower in REM than in non-REM sleep. (Price and Kremen, 1980). As already mentioned, Erwin and Buchwald (1986) have indicated that P1 in humans is markedly attenuated in non-REM sleep but returns to normal within REM. It is thus possible that while the MMN may not be visible in NREM, it may occur during REM sleep.

A recent study by Csepe, Karmos and Molnar (in press) suggests that MMN may exist in REM sleep in cats. They implanted electrodes in the primary auditory cortex (AI and AII) and above the association area (middle suprasylvian gyrus). Standard and deviant tone pips (4000 and 3000 Hz respectively) were presented at a 3/sec repetition rate. In different blocks, the probability of occurrence of the deviants was .50, .33, .30, .10 and .05. In the waking cat, an early broad-negative wave appearing between 30 and 70 msec recorded in the primary cortex discriminated between the standard and deviant stimuli. Like the human MMN, this amplitude of the cat MMN was inversely related to stimulus probability. Its appearance in the primary auditory cortex also agrees with neuromagnetic recordings of the MMN in humans (Hari et al., 1984). An MMN-like wave was seen in slow wave sleep (equivalent to stages 3 and 4 in humans). Its peak latency was prolonged compared to wakefulness but its amplitude was invariant, at least at lower deviant probabilities (.20 or less). The apparent cat MMN occurs nevertheless at a much earlier latency (approximately 50 msec) than in the human. Csepe

(personal communication with K. Campbell) has argued that cats are able to make sensory discriminations much earlier than humans. Both behavioural reaction times (Farley and Starr, 1983) and a physiological-like P3 (Csepe et al., in press) are much earlier in the cat than in the human suggesting information processing is much faster in the former than the latter.

Summary

Studies of evoked potentials suggest that manipulation of the subjects level of attention has a marked effect on components in the vertex N1 and P2 latency range. This is probably due to an overlapping "Processing Negativity" or "Nd". The effects of attention on temporal components, N1a and N1c are poorly understood. A later mismatch negativity (MMN) appears to be unaffected by manipulations of the subject's level of attention.

It is probably impossible for the waking subject to ever completely ignore irrelevant stimuli, regardless of instructions to that effect. In many instances (for example, when stimuli are loud or presented at a slow rate), evoked potential wave forms may not vary between attend and ignore conditions. Behaviourally, subjects may report at least some awareness of the unattended channel. Unfortunately, evoked potential researchers are forced to use circular argumentation to explain the presence of a particular attention-related wave form when subjects are apparently ignoring the evoking stimuli. Component X reflects the degree of attention (or "allocation of effort" or "degree of memory search") paid to a particular stimulus. The fact that wave form X is present when

subjects are not attentive is offered as proof that the subject was unable to ignore the stimulus. In short, the experimental effect and the dependent measure explain one another. At other times, researchers will claim that the presence of X in the unattended channel is a manifestation of the exogenous nature of the component. This makes the exogenous-endogenous distinction difficult. Manipulations of stimulus intensity or rate of presentation should affect the exogenous nature of N1. However, it could be equally argued that these manipulations will also affect the endogenous Processing Negativity or Nd. The same methodological concern affects our understanding of the MMN. Naatanen and his colleagues have argued that the MMN is independent of the subjects level of attention. Yet it is extremely difficult to test this hypothesis in the waking conscious subject who probably can never completely ignore external stimuli, however irrelevant. Perhaps the only time that normal subjects are least attentive is during natural sleep. Even when subjects are able to make sensory discriminations within sleep (as evidenced by behavioural responding), they rarely ever report awareness of stimulus presentations (Bonnet, Johnson and Webb, 1978).

The present thesis was therefore designed to employ sleep as a test of the exogenous-endogenous nature of the N1b-P2 complex and MMN. If N1b and P2 are at least partially exogenous, manipulation of the physical quality of the stimulus should have predictable effects on their amplitude and/or latency regardless of the level of arousal. Endogenous-related negativity on the other hand should be

largely removed in sleep. The MMN, an exogenous, automatic component should be unaffected by sleep. It should vary according to classical manipulation of the standard and deviant stimuli (e.g: probability of occurrence of the deviant and its degree of deviance from the standard).

Table 1.1

Author(s)	N	Stimuli	Electrodes	Stages	Components	Results
Anadeo and Shagas (1973)	3 M 5 F (21-46 yrs)	click (105 dB SPL, 0.1 msec duration, 200 msec ISI) -6 subjects tested 2 to 4 nights, 2 subjects tested during 8 hr waking session -2000 trials/average 2 trials/stage -clicks continuously presented all night	EEG (Cz-M1) EOG, EMG	wakefulness (PM & AM) and sleep stages 2, SWS (3 & 4) and REM	brainstem (waves I,II,III,IV) -amplitude measured from estimated base- line preceding stimulus	-no statistical differences in latencies and amplitude between wakefulness and sleep stages -waking latencies for waves I,II,III,IV: 1.61, 2.80, 3.71 and 5.56 msec. -sleep latencies slightly longer than in wakefulness -waking amplitudes for waves I,II,III,IV: 0.44, 0.49, 0.77 and 1.66 uV -they conclude sleep does not effect brainstem responses
Campbell and Bartoli (1985)	9 F (18-25 yrs)	clicks (standard condition: 70 dB nHL, 0.1 msec duration, 11/sec ISI) -rate of present- ation manipulation (11, 44 and 81/sec at 70 dB nHL) -standard condition recorded every 1/2 hour in sleep. In between the intensity and ISI manipulations were run in definite stages of sleep. -2 trials/stage for 11/sec ISI : 2000 clicks/trial 41/sec ISI : 4000 clicks/trial 81/sec ISI : 8000 clicks/trial	Cz, Oz referred to mastoid ipsilateral to ear of stimula- tion -EOG	wakefulness (PM) and sleep stages 2, 4 and REM -sleep stages scored online	brainstem (waves I-VI) -tympanic temperature recorded throughout the night	-temperature remained constant all night -peak latencies and amplitudes remained constant across stages of sleep and wakefulness -effects of rate of stimulus presentation and stimulus intensity were identical in the waking and sleeping subject
Ervin and Buchwald (1986)	7 M 7 F (22-25 yrs)	clicks (40 dB SL, 0.1 msec duration, 1 sec ISI) -presented through earphones fitted inside outer meatus	EEG (C2-M1+M2) EOG EMG	wakefulness and sleep stages 2,3,4 and REM -all subjects recorded in afternoon sleep -4 subjects recorded all night	-brainstem (wave V) -MLR (Pa, Nb) -late EP (Pi) -amplitudes measured from zero DC baseline	-wave V - no wake-sleep changes in latency or amplitude

Table 1.2

Author(s)	N	Stimuli	Electrodes	Stages	Components	Results
Erwin and Buchwald (1986)	7 M 7 F (22-25 yrs)	clicks (40 dB SL, 0.1 msec duration, 1 sec ISI) -presented through earphones fitted inside outer meatus -stimuli presented continuously -500 responses/average	EEG (Cz-M1+M2) EOG EMG	wakefulness and sleep stages 2,3,4 and REM -all subjects recorded in afternoon sleep -4 subjects recorded all night	-brainstem (wave V) -MLR (Pa, Nb) -late EP (P1) -amplitudes measured from zero DC baseline	-Pa -slightly later latency in NREM than in wakefulness -they state there were no changes in Na-Pa amplitude between wakefulness, NREM and REM sleep -Nb -could not be identified in NREM sleep -Nb in REM was similar to wakefulness
Mendel (1974)	3 M 3 F (20-31 yrs)	clicks (2 msec duration, 5/sec ISI) -intensity manipu- lation: -5 to 25 dB SPL in 5 dB steps -via loudspeaker 4 ft (3.3 m) from subject -512 trials/average -about 18 averages/intensity	EEG (Cz-A1, Cz-A2) EOG	light sleep (stages REM & 2) and deep sleep (stages 3 & 4) -stage determined online by "sleep stage analyzer"	MLR (Po,Na,Pa,Nb) -amplitude measured peak-to-peak -(note: latencies are measured much earlier in this study than in others)	Latency -more or less constant across the intensity levels Amplitudes -peak-to-peak latencies increased linearly with increases in intensity -no differences in latencies or amplitudes for light and deep sleep
Mendel and Goldstein (1971a)	1 M (26 yrs) 1 F (23 yrs)	clicks (50 dB SL, 0.4 msec duration, 9.6/sec ISI) -via loudspeaker 1 foot (0.3m) from subjects head -stimulus presentation while Ss awake and continued during sleep -average EP from 1024 responses	EEG (Cz-A1, Cz-A2) EOG	awake and sleep stages 1,2,3,4 & REM (determined offline) -testing occurred in 3rd & 4th consecutive night of sleep	MLR (Po, Pa) Amplitude: -Po to following negative peak (Na) -Na-Pa	Latency: -more or less constant across intensity levels: Amplitude: -Po-Na - slight decrease in REM and NREM, but not in drowsiness (stage 1) -Na-Pa - decrease in REM and NREM but not in drowsiness (stage 1)
Mendel and Goldstein (1971b)	2 F (22,28 yrs)	clicks (50 dB SL, 9.6/sec ISI) -via loudspeaker 1 foot from subjects head	EEG (Cz-A1, Cz-A2) EOG	awake and sleep stages 1,2,3,4 & REM (determined offline)	MLR (no quantification)	-stated there is little difference between wakefulness and light sleep -deeper stages of sleep are associated with a reduction in amplitudes -no components specifically identified
Mendel and Kupperman (1974b)	2 M 2 F (21-31 yrs)	clicks (50 dB SL, 1 msec duration, 1 sec ISI)	EEG (Cz-A1, Cz-A2) EOG	awake (pm), NREM (sleep stages 2,3,4) and REM -stage classification performed offline	MLR (Po,Na1,P,Na1, Pa,Nb) -amplitude measured peak-to-peak	Latencies: -Po - no difference between REM & NREM -Pa,Nb - latency shorter in REM than NREM Amplitude: -no statistical differences between stages

Table 1.3

Author(s)	N	Stimuli	Electrodes	Stages	Components	Results
Anch (1977)	3 (19-22 yrs)	tones (1000 Hz, 30 msec duration, 10 msec rise-fall, 1/sec ISI) -intensity manip- ulations: during wakefulness (45, 55,65,75 and 85 dB SPL) and sleep (50,65 and 80 dB SPL). -via earphones -240 trials/average -only 1 stimulus intensity presented during any 1 night -tones presented continuously and recording occurred only during definite stages of sleep	EEG (C3-A1) (C4-A2), EOG and EMG	-awake and sleep stages 2, SWS (364) and REM -Ss each slept 1 night a week over a 9 week period	-late (P1-N1)	-amplitude increased linearly with increase in intensity. -rough amplitude estimated from their Figure 4: wakefulness: 3.2 uV at 45 dB SPL, 6.2 uV at 85 dB SPL SWS & Stage 2: 2.5 uV at 50 dB SPL 4.0 uV at 80 dB SPL REM: 1.8 uV at 50 dB SPL 1.9 uV at 80 dB SPL -P1-N1 largest during wakefulness, smallest during REM -variance of amplitudes tended to increase with higher intensities.
Buchsbaum et al. (1975)	6 M 3 F (18-22 yrs)	click (1 msec duration, 1 sec ISI) -intensity manip- ulation (50,60,70 & 80 dB SPL) -via speaker on floor behind Ss head -64 clicks/condition -number of conditions per night not stated -4 intensities presented within each condition in "pseudo-random" order (4 intensities X 16 clicks per intensity)=64 clicks per intensity=64 clicks	EEG (Cz, reference site not indicated) EOG & EMG	awake and sleep stages 1,2,3,4 and REM -Ss slept 3 nights with testing on 2nd and 3rd nights	-late (compute value referred to as a mean deviation) -mean deviations obtained for latency windows for: P100 (76-112 msec), N140 (116-152 msec), P200 (168-248 msec), P300 (252-408 msec)	-stage 3 & 4 amplitudes were generally larger than in wakefulness -mean deviation amplitudes not reported for sleep stages 1,2 & REM except for P200 window -for P200, in stages 3 & 4 amplitude increased as a function of increasing intensity -mean deviations for 50 & 70 dB SPL stimuli were larger than for 60 & 80 dB SPL stimuli in wakefulness and sleep stages 1,2 & REM (their Figure 2)
Erwin and Buchwald (1986)	7 M 7 F (22-25 yrs)	clicks (40 dB SL, 0.1 msec duration, 1 sec ISI) -presented through earphones fitted inside outer meatus -stimuli presented continuously -500 responses/average	EEG (C2-M1+M2) EOG EMG	wakefulness and sleep stages 2,3,4 and REM -all subjects recorded in afternoon sleep -4 subjects recorded all night	-brainstem (wave V) -MLR (Pa, Nb) -late EP (P1) -amplitudes measured from zero DC baseline	-P1 -"disappeared" in NREM sleep; -P1 amplitude in REM was similar that in wakefulness

Fruhstorfer & Bergstrum (1968)	6 M 1 F (21-31 yrs)	click (60 dB SL, 1 msec duration, 8-20 sec ISI) -via loudspeaker (2 m in front of Ss head) -stimuli presented continuously and selectively, averaged offline	EEG : bipolar (5 electrodes along midline spaced 20% of nasion-inion distance starting 15% of distance above nasion (ie: about half the distance between Fpz-Fz, Fz-Cz, Cz-Pz, Pz-Oz, Oz-inion))	-daytime testing in natural sleep -awake, 4 levels of vigilance or drowsiness (ie: 4 qualitatively different phases of the EEG prior to sleep), light sleep (2 different EEG patterns) and sleep stages 2,3 and 4	-late (N1,P2,N2) -amplitude measures from average amplitude in 38 msec post-stimulus interval -components defined as maximum peaks within specific latency ranges: P1 (50-60 msec), N1a (80-90 msec), N1b (110-120 msec), P2a (180-190 msec), P2b (230-240 msec), N2 (300-310 msec)	-waking amplitudes: P1 (2 uV), N1a (12 uV), N1b (21 uV), P2a (8 uV), P2b (15 uV), N2 (4 uV) -P1 - no significant amplitude changes from wakefulness to sleep, slight increase (NS) in latency in sleep -N1 & P2 components decrease by 80% in very drowsy-light sleep stages -N1b, P2a,P2b: shorter latencies in sleep relative to wakefulness (only significant for P2a with 14 msec decrease) -N2 - significant increase in amplitude from wakefulness (4 uV) to sleep (about 17 uV) - large decrease in sleep latency (260-270 msec) from wakefulness
Kevanishvili and Specht (1979)	3	-tonepips (60 dB SPL, 1000 Hz, 8 msec rise-fall, 3.2 sec ISI) -click (60 dB SPL, 0.01 msec duration, 1/3.2 sec ISI) -via loudspeaker (1 m from Ss head) -50 responses/trial -number of trials per stage per S not known	EEG (Cz,C3 & C4 referred to left or right earlobes) EOG EMG	awake and sleep stages 1,2,3,4 & REM	late (P1,N1,P2,N2,P3) amplitude (P1-N1, N1-P2, P2-N2, N2-P3)	Amplitudes (to tones) -waking amplitude: P1-N1 (6.9 uV), N1-P2 (10 uV), P2-N2 (7.2 uV), N2-P3 (4.4 uV) -general decrease during sleep for P1-N1 and N1-P3 by 20-30% in stages 1 & 2, 70-90% in stages 3 & 4, 30-40% in REM sleep -general increase during sleep for P2-N2 and N2-P3 (range of increases from 7% to 200% with the largest percentage increase being for N2-P3) Latency (to tones) -waking latencies: P1 (61 msec), N1 (111 msec), P2 (188 msec), N2 (298 msec), P3 (407 msec) -general increase in latency in all stages of sleep with greatest increase occurring in stages 3 & 4, P1 (13-37% increase), N1 (15-54% increase), P2 (15-45% increase), N2 (11-53% increase), P3 (23-96% increase) Click stimuli: -P1, N1 and P2 latencies did not differ between -only N2 and P3 latencies showed significant increases from wakefulness to NREM sleep.

Ornitz et al (1967a)	3 M 3 F (21-36 yrs)	click (60 dB [reference not stated], 1 msec duration, 2.2-2.4 sec ISI -via loudspeaker 5 ft above Ss head -continuous stimulus presentation -averaging offline (100 clicks/trial))	EEG: Cz-O1, Cz-O2 EOG	stage 2 and REM across different times of night -REM was divided into periods of alocular quiescence and b) eye movement bursts	late (P2-N2)	-well defined P1, N1, P2 & N2 in their Figure 1 for a single subject -stage 2 amplitude: 2-14 uV REM amplitude: 5-12 uV -3 subjects: stage 2 > REM (4-8 uV difference, p<.05) 1 subject : stage 2 > REM (1 uV difference, NS) 2 subjects: stage 2 < REM (2-4 uV difference, NS) -authors state REM latency was significantly less than for stage 2 in 5 of 6 adults (no values were presented) -amplitude between S in REM periods: 2-18 uV (X=8 uV) 5 subjects: REM with no eye movement was greater than REM with eye movement
Ornitz et al. (1967b)	3 M 3 F (21-36 yrs)	click (60 dB [reference not stated], 1 msec duration, 2.2-2.4 sec ISI held constant across a night) -via loudspeaker 5 feet from Ss head	EEG (Cz-O1, Cz-O2) EOG	awake, drowsy, stage 2, SWS (stages 3 & 4)	late (P2-N2)	-waking latency not presented -sleep latency: 325 ms -P2-N2 amplitude: large within subject variations (4-44 uV) : largest single response recorded at or soon after sleep onset their figure 1 suggest amplitude stabilizes later in night.
Osterhammel et al. (1973)	8 M 3 F (22-74 yrs)	tone pips 2 sec ISI 1200 Hz intensity manip- ulation (5,10,20 30,40,50 dB SL) -via loudspeaker 1 m from Ss head -32 tones/average	EEG (Cz-M1)	awake light, medium & deep sleep (classified by the amount of delta activity occurring within 30 sec epochs)	-single subj. figure of EPs in wakefulness (50 dB SL), light sleep (20 dB SL), medium sleep (30 dB SL) & deep sleep (30 dB SL) -late EPs (N1, P2 & N2)	-latency of N1, P2, N2 : sleep > awake -amplitude N1-P2 : light sleep about = awake, decrease in medium sleep and largest in deep sleep. -amplitude P2-N2 : approximately double in light, medium & deep sleep as in wakefulness. -a large positive peak recorded in medium and deep sleep at about 700-800 msec.
Weitzman and Kremen (1965)	10 M	click (50 dB SL, 0.5 msec duration, 4 or 5 sec ISI) -via loudspeaker (2 ft [0.6 m] from subjects head)	EEG (Cz-right occiput) EOG	awake and sleep stages 2,3,4 & REM	late (P1, N1, P2, N2, P3) -peak-to-peak amplitude measurement (P1-N1, N1-P2, P2-N2 N2-P3) while P1 was measured from an "estimated" baseline -latencies measured at second peak	-results based on their figures 4 & 5 -P1: -latency in NREM and REM slightly later than wakefulness -amplitude in NREM slightly larger than in wakefulness -N1: -latency constant across wakefulness and sleep -amplitude (P1-N1) somewhat smaller in NREM and REM than in wakefulness -P2: -latency constant across wakefulness and sleep -amplitude (N1-P2) in REM was smaller than in wakefulness and SWS which in turn was smaller than in stage 2

Williams, Morlock & Lubin (1964)	3	click 80 dB SPL 1.6-2.0 sec ISI -via loudspeaker -continuously presented all night -100 to 300 responses/trial EEG only for 3 subj: B.D. (Cz-Oz) subj: F.R. (Fz,Cz, Pz,Oz referred to chin when awake & asleep. subj: B.U. (Cz referred to ear lobes)	awake & sleep stages 1,2,3,4 & REM	-late -subj. B.D.: (P1,M1,P2,N2) -subj. F.R. & B.U. pos. peak between 70-76 msec (P1), neg. peak between 100-130 msec (M1), pos. peak between 146-185 msec (P2) -also several pos. peaks before 70 msec but these varied with level of arousal.	-subj. B.D. -P1 & M2 were larger in NREM than wakefulness and REM -M1 & P2 were smaller in NREM than in wakefulness and REM -subj. F.R. -general reduction in all peak-to-peak amplitudes between wakefulness (their figure 2) and stage 4 (their figure 4) -subj. B.U. -early positive peaks disappear in sleep -waking positive peak at 76 msec (P1) occurred earlier in stage 2 at 56 msec (their figure 3). P2 appeared earlier in stage 2 at 146 msec than in wakefulness at 185 msec. Its amplitude (presumably from electronic zero) decreased in sleep.
Williams, Tepas and Morlock (1962)	3 M	click (85 dB SPL, EEG (Cz-O1) 1 click/sec ISI) -via loudspeaker (1 foot (0.3 m) from subjects head) -100 responses/trial -stimuli presented continuously all night	awake and sleep stages 1,2,3,4 and REM -stage classification done offline.	-late (P1,M1,P2,N2) -"baseline" (electronic zero)-to-peak except for P2-N2	-P1 increased in amplitude during sleep with greatest effect in SWS -M1 and P2 increased in amplitude in sleep with greatest effect in SWS

Chapter 2

The Auditory Evoked Potential During Sleep: N1 and P2

Introduction

A review of the literature has pointed to the dual exogenous-endogenous nature of the vertex N1-P2 complex. Manipulations of the qualities of the physical stimulus have marked effects on its morphology. On the other hand N1-P2 are also effected by psychological manipulations such as the subject's level of attention. Unfortunately many of the manipulations of the physical qualities of the evoking stimulus may be confounded by attentional effects. For example, as the stimulus becomes more intense or its rate of presentation becomes slowed, it becomes increasingly difficult to ignore it. The change in N1-P2 might thus be due to either the intended manipulation of the physical stimulus or the unintended manipulation of the state of attentiveness.

Differences between attended and unattended stimuli may be assessed through subtraction wave forms such as the Processing Negativity or "Nd". This tells us little about the fate of the unattended channel. The N1-P2 that is typically seen following to-be-ignored stimuli might be a true exogenous effect or it might be evidence of a partial Processing Negativity. Neither the "raw" N1-P2 complex nor the difference wave form can provide us with an absolute indication of the amount of processing that occurs in an

unattended channel before it is ultimately rejected from consciousness. The difference wave form provides an index of the amount of processing an attended channel receives relative to when it is not attended. It is probably impossible for the waking subjects to ever completely ignore any stimulus that arrives at the receptor. As such the degree to which the N1-P2 complex reflects exogenous or endogenous processes may not be possible to test in the waking subject.

The first experiment therefore employed sleep as an experimental manipulation. It was thought that sleep would be the period in which endogenous factors (such as attention) would be best removed. Sleep is not however a unitary phenomenon. In addition to the apparent physiological differences among the various stages, it is also thought that information is differentially processed within these stages. "Gating" of external stimuli appears to be most likely in slow wave sleep and least likely in stage REM. For these reasons, comparisons were made between wakefulness and sleep, but also among the various stages within sleep. If the N1-P2 complex is largely exogenous, it should be unaltered by sleep. On the other hand, if it is largely endogenous, it should be markedly attenuated by sleep.

Since the N1-P2 complex is known to be affected by stimulus parameters, two classical manipulations were carried out. In the first, stimulus intensity was altered. The waking N1-P2 was expected to be larger following high compared to low intensity stimuli. In the second, the rate of stimulus presentation was

slowed. The N1-P2 was expected to be larger when the stimuli are presented at slow compared to a fast rate. Again, if the N1-P2 complex is largely exogenous, manipulations of the physical stimulus should have identical effects in the waking and sleeping subject.

N1 appears to consist of a series of sub-components labelled N1a, N1b and N1c. N1a and N1c appear in temporal sites at earlier and later latencies than the vertex-maximum N1b. Little is known about N1a. By contrast, N1c appears to fit into the "exogenous" classification in that it is affected by the ear of stimulation. Following monaural stimulus presentation, N1c is larger over the contralateral than the ipsilateral temporal region. However, there is also some evidence that N1c is also affected by manipulations of the subject's level of attention. To resolve this controversy, stimuli were presented monaurally to the left and right ears in wakefulness and sleep. Again consistent with the previous hypotheses for N1-P2, if N1a and N1c are largely exogenous in nature, they should be minimally affected by sleep.

Methods

Subjects

Two males and 8 females (22-35 years old) with no reported hearing disabilities volunteered to participate in this study. Subjects arrived approximately two hours before their normal bedtime during which time electrodes were affixed and baseline testing took place. They were told to refrain from drinking coffee or alcohol or

taking any drugs within 24 hours of testing. They were tested over two consecutive nights in the sleep laboratory. Five subjects had previously participated in sleep research.

Procedure

All subjects were tested in a "Standard" condition and in four variations of this condition. In the standard condition, trains of 80 dB SPL, 1000 Hz tone pips 55 msec in total duration (5 msec rise-and-fall times) were binaurally presented at an inter-stimulus interval (ISI) of 1100 msec. Stimuli were delivered by a specially designed (Starkey Laboratories Inc.) behind-the-ear hearing-aid device. Speaker output, from a Knowles ED-197 wide bandpass receiver, was conducted through the earhook (about 5 cm long) of the hearing aid which in turn was connected to 4 cm of no. 13 standardized tubing (1.93 mm in diameter). Individually fitted ear moulds were attached to the end of the standardized tubing. Both ears were fitted with an ear mould. The snug-fitting ear moulds assured constancy of auditory input in the sleeping subject in spite of possible changes in head or body movements. This system was calibrated using a Bruel and Kjaer 2209 sound level meter and a 2 c.c coupler. A 0.2 V RMS input signal produced a relatively flat response (94-100 dB SPL) from 100 to 4000 Hz.

Four variations of this standard condition were presented by varying one of the stimulus parameters while holding all others constant. Since the N1 and P2 evoked potentials are affected by the physical qualities of the stimulus, each of these manipulations was expected to have a predictable effect on the wave form. In the

second "Low Intensity" condition, stimulus intensity was lowered from 80 to 50 dB SPL. This was expected to result in an attenuation of the the N1-P2 complex (Davis et al., 1966). In the third "Long ISI" condition, the ISI was increased to 3300 msec. This was expected to result in an increase in the amplitude of the N1-P2 complex (Davis et al., 1966; Nelson and Lassman, 1968; Perrault and Picton, 1984a). In a fourth "Left Ear" condition, stimuli were presented monaurally to the left ear and in a fifth "Right Ear" condition, monaurally but to the right ear. This was expected to produce differential effects on the N1a and N1c components between the contralateral and ipsilateral temporal sites (T3 and T4). Two hundred stimuli were presented per condition in all but the long ISI condition. In this condition 50 stimuli were presented.

Subjects were tested in a sound attenuated sleep laboratory. Prior to sleep subjects were asked to lie on their backs and read a book. This assured a high level of arousal. The EOG was monitored to ensure subjects continued to read. They were tested in the standard condition and the four variations of it. Upon completion of the baseline testing, the lights were turned off and the subjects were allowed to fall asleep. Stimulus presentation began about 5 minutes after the subject had entered definite stage 2 or 4 of sleep. Six subjects were further tested in the standard condition in the morning after they were awakened. Two blocks of stimuli were recorded for each condition during wakefulness and when possible, during the different sleep stages to insure replicability of the results.

Physiological Recording

Electroencephalographic (EEG) and electro-oculogram (EOG) activity were recorded using Beckman gold electrodes attached to the scalp (10-20 system) with collodion soaked gauze. The EEG was recorded from electrodes placed at Fz, Cz, Pz, T3 and T4 and referenced to a balanced non-cerebral sterno-vertebral site (Stephenson and Gibbs, 1951). EOG electrodes were placed on the supra-orbital ridge of the left eye and the infra-orbital ridge of the right eye. This permitted the recording of horizontal and vertical eye movements on a single polygraphic channel. Interelectrode impedance was below 5 Kohm. EEG and EOG signals were recorded using Nihon-Kohden EU/50 amplifiers with a high filter setting of 25 Hz and a time constant of 0.3 sec. EEG and EOG activity were also written out on paper at a speed of 10 cm/sec. The different stages of sleep were classified by an experienced rater according to the criteria of Rechtschaffen and Kales (1968). Testing occurred in the evening before subjects slept (pre-sleep wakefulness) and during definite sleep stages 2, 3, 4 and REM. Stage 2 was divided into early and late halves to examine possible time-of-night effects. Stages 3 and 4 were combined to form slow wave sleep (SWS). In cases of stage ambiguity, the records were later scored by a second, experienced rater. If the two raters disagreed, the condition was rejected from further analysis. Fewer than 5% of the conditions were rejected for this reason. Signal recording was discontinued and rejected when the EEG sleep pattern showed signs of a stage change or muscle artifact.

Data collection was controlled by a Z-2 Cromemco micro-computer equipped with a 12 bit analogue-to-digital converter (Maskare, Campbell, Stelmack and Knott, 1985). Online averaging of the EEG began 100 msec prior to stimulus onset and continued for 600 msec (i.e. 500 msec post-stimulus) using a 2 msec dwell time. Trials in which the EOG or Fz activity exceeded ± 100 μ V were automatically rejected from the ongoing average. Such artifact occurred typically as a result of eye movement in wakefulness and stage REM. Trials "contaminated" by high amplitude frontal K-Complexes often appearing in non-REM sleep were therefore rejected. All evoked potentials were stored on floppy disk for subsequent offline plotting and analysis.

Evoked Potential Analysis

Components of the evoked potential wave forms were computer-identified as the largest negative or positive deflections appearing within specific time intervals (see Bell, Campbell and Deacon-Elliott, Appendix 1 of this thesis for a description of the scoring algorithm). The latency and amplitude of P1, N1, P2 and N2 were identified as the maximum peaks at Cz within the following time intervals: P1 (30-80 msec); N1 (70-130 msec); P2 (140-220 msec) and N2 (200-400 msec). Values obtained at other electrodes were taken at the peak latency of the Cz data. Peak amplitudes were measured relative to the average of the 100 msec pre-stimulus activity. For most subjects, N1a and N1c were often not distinguishable within sleep and for some, during wakefulness. An alternate scoring method was thus employed for these sub-components. The wave forms were

quantified by computing the mean amplitude of data points falling within latency windows for which these components have been reported in the literature. The latency windows used were 70-90 msec for N1a, 90-120 msec for N1b and 120-150 msec for N1c. The window for N1a (20 msec) was shorter than the other windows to minimize the possibility of averaging data related to P1 processes.

The time spent in the various stages of sleep varied from subject to subject. For this reason, not all subjects could be run in all conditions in all stages of sleep. For the standard condition, complete data were obtained for nine subjects in all stages of sleep. One subject did not remain long enough in SWS to be tested. There were no subjects in the long ISI, left ear, right ear or low intensity conditions with complete data across the different stages of sleep. The number of subjects having data in three of four stages in these conditions were nine, eight, seven and five respectively. Since data were analysed using the BMDP statistical computer package (P2V), a subject was included into a repeated measures analysis of variance (ANOVA) only if he/she had complete data for the variables entered for the comparison under consideration. In the standard condition, there were sufficient data (nine subjects) to permit a comparison across early stage 2, SWS, late stage 2 and REM. In the other conditions, to minimize the number of subjects excluded from the analyses, it was necessary to collapse across early stage 2, SWS and late stage 2 to form non-REM (NREM) sleep. As such, NREM data were obtained for all ten subjects in the long ISI, left and right ear conditions. In stage REM, data

were available for seven subjects in the long ISI condition, and eight subjects in both the left ear and right ear conditions. The number of subjects included in an analysis of these conditions was therefore determined by the number of subjects for which stage REM data were available. In the low intensity condition, data for NREM (combined early stage 2, SWS and late stage 2) were available for eight subjects. REM data was only available for three subjects in and hence was not included in the low intensity analysis.

For the standard condition, a series of one-way repeated measures ANOVAs were run to compare the latencies and amplitudes of P1, N1, P2 and N2 at Cz between wakefulness (pre-sleep), early stage 2, SWS, late stage 2 and REM. To verify consistency of the evoked potential in wakefulness, these variables were compared during evening (pre-sleep) and morning (post-sleep) wakefulness. A t-test for correlated means was employed. The effect of intensity was assessed by computing separate Intensity by Stage repeated measure ANOVAs for the latency and amplitudes of P1, N1, P2 and N2 at Cz. Similarly a separate ISI by Stage repeated measure ANOVA was computed for the latency and amplitudes of these components at Cz. The standard condition served in the former analyses as the high intensity condition while in the latter analyses, it served as the short ISI condition.

The mean amplitudes in windows corresponding to N1a, N1b and N1c were examined to determine whether they changed from wakefulness to sleep. This was assessed by computing separate Ear by Stage repeated measure ANOVAs for T3 and T4 data. To examine ipsilateral

versus contralateral effects, an Ear by Electrode (T3,T4) repeated measure ANOVA was conducted on the transformed data (see next paragraph) of N1a and N1c during pre-sleep wakefulness, NREM sleep and REM sleep.

In the standard condition, topographical variation of P1, N1, P2 and N2 was examined in separate analyses. In the past this has generally been performed using a Condition by Electrode repeated measures ANOVA. McCarthy and Woods (1984) have argued that such a procedure is statistically incorrect. An assumption of the ANOVA model is that conditional effects are additive. Across electrode sites the effects are however multiplicative rather than additive. As an example, assume that in a baseline condition the amplitude at electrode site X is 10 uV while at site Y, it is 15 uV. Under the effects of an experimental condition, the amplitude of X increases to 20 uV (an increase of 10 uV). If the amplitude at Y increases by a multiple of 2 (or to 30 uV for an increase of 15 uV), a Condition by Electrode interaction would be implied. Although the experimental effect on both X and Y is identical in terms of doubling their amplitudes, according to the additive assumption of the ANOVA model, the effect is greater at Y than at X. To overcome this problem, McCarthy and Woods recommend that the raw amplitude data be transformed. Their transformation algorithm was employed in this study for the standard condition. Within wakefulness and each stage of sleep, the minimum and maximum amplitude at Fz, Cz and Pz grand averaged data were computed. For each subject, in each stage the various components were transformed by subtracting the

corresponding minimum amplitude (calculated from the grand average) from the raw data and then dividing by the difference between the corresponding maximum and minimum grand average amplitudes. A separate Stage by Electrode repeated measure ANOVA was conducted on the transformed amplitudes of P1, N1, P2 and N2 in the standard condition. The Electrode factor consisted of three sites (Fz, Cz and Pz).

In order to better illustrate the difference between the waking and sleeping evoked potentials, subtraction wave forms were computed by subtracting, point by point, the sleep from the waking wave forms recorded in the same condition (Naatanen et al., 1978, 1980a; Hansen and Hillyard, 1980, 1983, 1984). The five difference wave forms computed in the standard condition were: 1) wakefulness (pre-sleep) minus early stage 2; 2) wakefulness minus SWS; 3) wakefulness minus late stage 2; 4) wakefulness minus REM and 5) pre-sleep wakefulness minus post-sleep wakefulness. For the long ISI, left and right ear conditions, two difference wave forms were computed: wakefulness minus NREM and wakefulness minus REM. Since there were insufficient REM data for the low intensity condition, only the wakefulness minus NREM difference wave forms were computed. The subtraction wave form served only to define at what point in time waking and sleeping evoked potentials first differed. The onset latency of the difference wave form was measured at the point at which when the leading edge of the difference wave form equalled 25% of it's maximum negativity (Hansen and Hillyard, 1980). The onset latency in each of the difference wave forms in the standard condition was

compared using a one-way repeated measures ANOVA at Fz and Cz data where "Nd" is largest (Hansen and Hillyard, 1980). The data were also collapsed to form NREM data in this condition in order to allow comparisons with the low intensity and long ISI conditions. A one-way repeated measure ANOVA was used to contrast the onset latency of the low intensity difference wave form (awake-NREM) with the high intensity (i.e. standard) difference wave form. To compare the onset latency of the two difference wave forms in the long ISI condition with those in the short ISI (ie: standard) condition, a two-way ANOVA was performed at Fz and Cz with repeated measures on level of arousal (awake-NREM, awake-REM) and ISI (short, long).

Post-hoc analyses of main effects were performed using Tukey's Honestly Significant (HSD) test of significance. Isolation of interaction effects were conducted using the 'Treatment-Contrast' and 'Contrast-Contrast' procedures described by Kirk (1982).

Results

Standard Condition

Figure 2.1 represents the superimposed wave forms for all subjects recorded in the standard stimuli during wakefulness and the different stages of sleep. It may be observed that the effects of sleep are, in general, consistent across all subjects.

----- Insert Figure 2.1 here -----

The average peak latency of P1 at Cz was 46 msec. The

amplitude at Cz (1.04 uV) was only slightly larger than at Fz (0.97 uV) and Pz (0.93 uV). N1 peaked at an average latency of 100 msec in wakefulness and had a fronto-central distribution. It was largest at Cz (-5.67 uV) and Fz (-5.01 uV) with the smallest amplitude occurring at Pz (-3.39 uV). The waking P2 occurred at an average latency of 197 msec. It had a more posterior distribution than N1 being maximum at Cz (3.56 uV) and declining in amplitude at Fz (1.75 uV) and Pz (1.87 uV). The N2 component had an average latency of 292 msec and also had a fronto-central distribution. Its amplitude was -2.22 uV at Fz, -2.64 uV at Cz and -1.04 uV at Pz. The grand average wave forms from the standard condition are shown in the upper half of Figure 2.2. The average latency and amplitude of P1, N1, P2 and N2 recorded in the standard condition are presented in Table 2.1.

----- Insert Figure 2.2 and Table 2.1 here -----

P1 latency was significantly different across the stages of sleep and wakefulness ($F(4,32)=3.20$, $p<.01$). Although it occurred 5 to 22 msec later in sleep relative to wakefulness, the delay was only found to be significant in SWS ($q(5,32)=5.19$, $t<.05$). The main effect of level of arousal on the latency of N1 approached significance ($F(4,32)=2.61$, $p=.053$). It was delayed 7 to 18 msec during sleep with the delay being greatest during S2E and REM sleep.

P2 latency remained relatively constant throughout the night. N2 occurred 17 to 53 msec later in sleep than in wakefulness ($F(4,32)=$

3.29, $p < .05$). Only during SWS was N2 latency statistically later than during pre-sleep wakefulness ($q(5,32) = 53.89$, $t < .05$).

In general, the amplitudes of P1, P2 and N2 were larger during sleep than during wakefulness whereas N1 was smaller during sleep. However, the main effects for P1 and P2 only approached statistical significance (P1: $F(4,32) = 2.54$, $p = .058$; P2: $F(4,32) = 2.48$, $p = .063$).

On the other hand, N1 and N2 main effects were both statistically significant (N1: $F(4,32) = 23.07$, $p < .01$; N2: $F(4,32) = 13.15$, $p < .01$). Post-hoc analyses revealed that N1 amplitude during SWS and late stage 2 was statistically reduced compared to wakefulness (SWS: $q(5,40) = 11.50$, $t < .01$; Stage 2 late: $q(5,40) = 11.64$, $t < .01$). The N1 observed in REM, although attenuated, did not significantly differ from that seen in wakefulness. Similarly the REM N1 did not significantly vary from that seen in early or late stage 2 or SWS. N1 often appeared to be at or below baseline levels in NREM sleep and slightly above in REM sleep. To determine whether N1 significantly deviated from the pre-stimulus baseline, 95% confidence intervals were computed for wakefulness and sleep data. N1 did not statistically deviate from baseline (i.e. did not exceed 0 uV) in SWS and late stage 2. With regards to the main effect of arousal for N2, the amplitude during early stage 2 was larger than in wakefulness ($q(5,40) = 5.28$, $t < .01$) and REM sleep ($q(5,40) = 4.60$, $t < .05$).

Table 2.2 presents the average amplitude of the late auditory components across the sleep stages in the standard condition at Fz, Cz and Pz. During wakefulness the amplitude of P1 was about the

same at Fz, Cz and Pz. An analysis of the effects of sleep on the "normalized" (transformed) data failed to reveal a change of P1 topography within sleep.

----- Insert Table 2.2 here -----

N1 in wakefulness was largest at Cz decreasing by 1% at Fz and 40% at Pz. A significant Electrode Site by Stage interaction was revealed for the transformed data ($F(8,64)=5.70$, $p<.01$). The N1 treatment-contrast analysis revealed significant interactions between Fz-Pz and the STAGE factor as well as between Cz-Pz and the STAGE factor. In order to identify at what stages of sleep or wakefulness the interactions were occurring, a contrast-contrast analysis was further conducted. The direction of amplitude change in N1 between Fz and Pz during SWS as well as during late stage 2, was opposite to that recorded during stage REM sleep ($p<.05$) and wakefulness. N1 amplitude was more negative at Pz than at Fz in SWS and late stage 2, whereas N1 was more negative at Fz than Pz during REM sleep. Although N1 was found to be more negative at Fz than Pz during wakefulness and early stage 2, the interactions only approached significance.

The N1 Cz-Pz by Stage interaction was similarly due to N1 being more negative at Cz than at Pz in wakefulness, early stage 2 and REM whereas in SWS and late stage 2, it was more negative at Pz than Cz.

The contrast-contrast analysis, however, only approached significance in spite of the overall significant interaction.

Although incomplete data would not permit an analysis to be conducted across the four stages of sleep for either the long ISI or low intensity conditions, the data also revealed similar effects were observed in these conditions. In the long ISI condition, the amplitude of N1 was also more negative at Pz than Cz in early stage 2.

The P2 component was largest at Cz in wakefulness and decreased by about 50% at Fz and Pz. No statistical changes in topography were found in sleep. While P2 was maximum at Cz in all stages of sleep the decrease at Fz and Pz was not as large in sleep - the range being from 21 to 31%. The topography of N2 did not vary between wakefulness and sleep. It was largest at Cz in all stages, decreasing in wakefulness by 15% at Fz and 60% at Pz, and from 16 to 40% at Fz and Pz in sleep.

The lower half of Figure 2.2 represent subtraction wave forms for the standard condition. There were no statistical differences for the onset latency between these wave forms at Fz or Cz. The onset latency was found to be 50 msec in early stage 2, late stage 2 and REM difference wave forms, and 56 msec in the SWS difference wave form.

Stimulus Intensity

As mentioned, the low intensity condition was run in stage REM for only three subjects. Thus comparisons in both the high and low intensity conditions were based on NREM sleep (collapsed across stages) versus wakefulness. The grand average wave forms from the low intensity condition are shown in Figure 2.3. The mean latencies

and amplitudes of P1, N1, P2 and N2 recorded in the low and high intensity conditions are presented in Table 2.4. There were no differences in the latency of these components following changes in stimulus intensity. A significant Stage main effect was found for the latency of P1 ($F(1,7)=6.43$, $p<.05$) and N2 ($F(1,7)=12.29$, $p<.01$). They were delayed in NREM sleep (P1: 59 msec; N2: 342 msec) compared to wakefulness (P1: 46 msec; N2: 293 msec). A significant Intensity by Stage interaction was found for P2 latency ($F(1,7)=6.01$, $p<.05$). The latency of P2 to the low intensity stimuli occurred earlier in wakefulness (177 msec) than in NREM sleep (199 msec) whereas in the high intensity condition it occurred earlier in NREM sleep (190 msec) than in wakefulness (197 msec).

----- Insert Figure 2.3 and Table 2.4 here -----

Significant main effects of Intensity and Stage were found for the amplitudes of N1, P2 and N2. N1 and P2 were smaller in the low than high intensity condition (N1: $F(1,7)=19.81$, $p<.01$; P2: $F(1,7)=6.82$, $p<.05$). N1 was also larger in wakefulness than NREM ($F(1,7)=76.39$, $p<.01$). P2 was not significantly affected by sleep ($F(1,7)=2.01$, $p=.20$). N2, on the other hand, increased in amplitude during NREM sleep compared to wakefulness ($F(1,7)=13.46$, $p<.01$). There were no significant interactions for the amplitude any of these components.

The low intensity manipulation was also carried out in three subjects in REM sleep. Because of the small sample size only

descriptive statistics can be presented. However, it is apparent from Figure 2.3 that P1 and P2 in REM are larger than in wakefulness. The REM P2 was somewhat larger than P2 in NREM. N1 was larger in REM than NREM occupying an intermediate position from wakefulness to NREM sleep. Similar results were apparent when waking and NREM grand averages were constructed for only these three subjects.

The difference wave forms for the low intensity condition are shown in the lower half of Figure 2.3. No statistical effects were found for the onset latency between the low (Fz: 58 msec; Cz: 67 msec) and high intensity conditions (Fz: 58 msec; Cz: 60 msec).

Rate of Stimulus Presentation

The grand average and subtraction wave forms for the long ISI condition are shown in Figure 2.4. The mean amplitude of the late auditory components are presented in Table 2.4. The latency of P1, N1, P2 and N2 did not vary between the short and long ISI conditions. The only statistical differences in latency were obtained for the Stage main effect for N2 ($F(2,12)=8.92$, $p<.01$). The peak latency of N2 occurred later in NREM sleep than during wakefulness ($q(3,12)=4.16$, $t<.05$). Its latency during wakefulness, NREM and REM sleep was 300 msec, 345 msec and 315 msec respectively.

Although a similar trend was observed for both N1 and P2, the differences were not significant.

----- Insert Figure 2.4 and Table 2.4 here -----

The amplitude of P1 was not significantly altered by manipulation of the ISI. A significant main effect of Stage of sleep was found ($F(2,12)=6.42$, $p=.013$). The NREM P1 (3.31 μV) was more positive than the waking P1 (1.20 μV) ($q(3,12)=4.56$, $t<.05$). Although P1 was also more positive in REM sleep than in wakefulness this was not statistically significant. An ISI by Stage interaction was obtained for both N1 and P2 amplitudes. In wakefulness and REM, N1 was smaller in the short than long ISI condition. The opposite was found during NREM sleep where N1 was smaller in the long than short ISI condition. The amplitude of P2 in the long ISI condition was larger in NREM than in REM or wakefulness while in the short ISI condition no changes were found in P2. ISI and STAGE main effects were also found for N2. The longer ISI elicited a larger N2 than the shorter ISI ($F(1,6)=22.65$, $p<.01$). In addition, the NREM N2 was larger than both the waking and REM N2 ($q(3,12)=6.14$, $t<.01$). The Stage by ISI interaction was not significant.

Neither main effects nor interactions were found in the ISI by Stage ANOVA for the onset latency in the difference wave form. The onset latencies were found to occur from 40 to 55 msec.

Ear of Presentation

This set of analyses addressed the question of whether signal activity in the windows corresponding to N1a, N1b and N1c (the components being determined by averaging of the amplitude within defined windows rather than being based on a peak amplitude per se) varied with the stage of sleep and ear of stimulus presentation. The grand average and subtraction wave forms for the left and right

ears are presented in Figures 2.5 and 2.6 respectively. Mean amplitudes in the intervals corresponding to N1a, N1b and N1c are shown in Table 2.5.

At T3 a significant main effect of Stage was found for the amplitude of N1a ($F(2,10)=6.96$, $p<.01$). It was larger (more negative) in wakefulness than in NREM and REM sleep although the difference only reached significance for NREM sleep ($q(3,10)=1.08$, $t<.05$). At T4, N1a was also larger in wakefulness than NREM and REM but none of the differences reached significance. The amplitudes of N1b and N1c at T3 and T4 were larger in wakefulness than in either NREM or REM sleep but these differences did not reach significance.

----- Insert Figures 2.5 and 2.6 here -----

Insert Table 2.6 here

The main effect of ear of presentation was not found to be significant for either N1a or N1c in wakefulness, NREM sleep or REM sleep. The Electrode main effect for N1a in wakefulness approached significance ($F(1,7)=5.11$, $p<.06$) with the amplitude at T3 being more negative than at T4. No other significant effects were found in this set of analyses. A significant Ear by Electrode site interaction was found for N1c during wakefulness ($F(1,7)=7.62$, $p<.05$) and NREM sleep ($F(1,7)=7.35$, $p<.05$). In wakefulness, N1c was larger at T4 than T3 to left ear stimulation whereas it was larger at T3 than T4 for right ear stimulation. No significant differences were found in sleep. In NREM sleep, N1c was larger at T3 than T4

for both left and right ear stimulation. In REM sleep, N1c was larger at T3 than T4 for left ear stimulation while for right ear stimulation, it was larger at T4 than T3.

DISCUSSION

The evoked potential wave forms recorded to stimuli in wakefulness are consistent with results reported in the literature. Both N1 and P2 increased in amplitude from the low to high intensity (i.e., "standard") conditions, replicating a number of previous reports (Davis et al., 1966; Nelson and Lassman, 1968; Picton et al., 1978). Similarly, the increase in N1 and P2 amplitude at the slower rate of stimulus presentation is consistent with previous observations (Davis and Zerlin, 1966; Nelson and Lassman, 1968; Picton et al., 1974, 1978; Perrault and Picton, 1984a). During wakefulness, N1 across all conditions displayed a fronto-central scalp distribution with maximum amplitudes at Cz. The topography of P1 and P2 was slightly more posterior than N1 (Picton et al., 1974; Simpson et al., 1976, 1977; Peronnet and Michel, 1977; Streletz et al., 1977; Wolpaw and Woods, 1982). At temporal electrode sites (T3, T4), N1a- and N1c-like components were visible following monaural presentation of the stimulus and to a lesser extent when stimuli were presented binaurally (i.e., during the standard, low intensity and long ISI conditions). N1a did not discriminate between the ear of presentation of the stimulus. This is in agreement with the majority of studies in the literature (Wolpaw and

Penry, 1975; McCallum and Curry 1980; Perrault and Picton 1984a; Woods et al., 1986). Following left ear stimulus presentation, the later N1c was larger over the right than the left temporal area. There were no significant amplitude differences between left and right sites following stimulus presentation to the right ear. Perrault and Picton (1984a) have also reported N1c asymmetry to left ear, but not right ear presentation.

During wakefulness, the various experimental manipulations produced results that were highly consistent with the literature regardless of the component under consideration. It may be concluded therefore that although an unusual stimulus transducer was employed (a hearing-aid device), it had minimal effect on the evoked potential morphology or its characteristics.

The effects of the manipulations of the physical parameters of the stimulus (rate, intensity) suggest that the late components of the auditory evoked potential may be exogenous in nature. It might be equally be argued that that such apparently exogenous manipulations were, in reality, altering the psychological state of the subject -- their level of attentiveness. Increasing stimulus intensity or slowing its rate of presentation increases the likelihood that the subject will passively attend to the stimulus (Schwent et al., 1976a,b). N1c asymmetry in temporal regions have also been at least partially explained as an endogenous effect of attention (Perrault and Picton, 1984a). For these reasons, subjects in the present study were tested in the period when they were least attentive -- during natural sleep.

Difference Wave Forms

The differences between wakefulness and sleep are best seen in the "difference" wave form, obtained by subtracting the sleeping from the waking wave forms in identical conditions. This technique removes those portions of the evoked potential which are common to both sleep and wakefulness. Hence, the difference wave form may serve as an index of the additional processing of stimuli that occurred within wakefulness. An examination of the difference wave forms showed a slow negative component began about 30 to 50 msec after stimulus onset and continued for several hundred msec. The onset of the difference wave form was defined at the latency at which it exceeded 25% of its maximum peak. It is therefore likely that its true onset began several msec before. Difference in processing between sleeping and waking may therefore begin as early as 20 to 40 msec after stimulus onset. This is within the range of the middle components, where, as mentioned in the first chapter, results have been equivocal. Differences in the auditory evoked potential as a result of selective attention have recently been reported in this latency range (McCallum, Curry, Cooper, Pocock, and Papakostopolous, 1983; Woldorff, Hansen and Hillyard, 1986). Woldorff et al. observed a positive shift in mid-latency components whereas a negative shift was observed in the present study. They suggested the early (20 msec) onset of Nd in the traditional dichotic listening task reflected a selective "tuning" or "biasing" since there would have been insufficient time for a complete perceptual analysis. The early difference in negativity observed in

the present study may suggest, in contrast, that initial perceptual processing could begin soon after stimulus onset in the sleeping subject. It is also possible that a tonically maintained pre-stimulus set is established in the sleeping subject to permit rapid rejection of irrelevant stimuli (Naatanen and Michie, 1979). Such pre-stimulus sets presumably would permit the rapid "gating" of all external stimuli, however relevant. A pre-stimulus set would nevertheless be unable to explain how highly relevant, informative stimuli manage to evoke later K-complexes (Oswald, Taylor and Treisman, 1960). The rejection process began earliest for stimuli that were loud and presented at a slow rate and was delayed for low intensity stimuli presented at a relatively fast rate.

The difference wave form was sustained for a relatively long period of time and overlapped the P1, N1 and P2 waking wave forms. The morphology of the sleeping-waking difference wave forms appear to be similar to "Processing Negativity" or "Nd" wave forms observed in many of the studies of selective attention. In these studies, Nd differentiates between a stimulus when it is attended and when it is not attended (Naatanen et al., 1978, 1980a; Hansen and Hillyard, 1980). The present difference wave appeared to consist of two negative deflections followed by a slow positivity. Although the peak latencies and amplitudes of the subtraction wave forms were not quantified, the first negative deflection occurred at about the peak latency of the N1 component in the grand average wave forms and the second occurred slightly beyond the peak latency of P2. The Nd wave form has also been reported to consist of two sub-components. The

data by Hansen and Hillyard (1980) and Naatanen et al. (1981) suggest the Nd sub-components appeared about 100 to 200 msec later than the first and second negative deflections observed in the subtraction wave forms in this study. Naatanen et al. (1981) reported that the first sub-component (2 uV) was much smaller than the second later sub-component (5-10 uV). Depending on the ease of rejection of the unattended channel, the amplitude of the two sub-components may vary (Hansen and Hillyard, 1980). In the present study, the first negativity was larger than the second. Consistent with the early onset of the present difference wave, the high amplitude first negativity probably reflects a relatively rapid rejection of irrelevant information during sleep.

The Nd wave form is a measure of the extent to which an attended stimulus receives additional processing than when it is not attended. Looking at this from another view, the Nd reflects the extent to which irrelevant, unattended information is not processed or is "filtered". Like Nd, it is suggested that the difference wave forms in this study provides a measure of the extent to which stimuli receive additional processing during wakefulness compared to sleep. This slow negative difference wave will be called "wNd" (difference in negativity due to wakefulness) to distinguish it from the Nd described in dichotic listening tasks.

The P1 Component

The main effects of stimulus intensity, rate of presentation and ear of presentation had no significant influence on P1 latency. On the other hand, there were relatively large changes in the

latency and amplitude of the P1 component within sleep, independent of stimulus parameters. In sleep, P1 was delayed by as much as 22 msec in the standard condition with similar effects also being found in the low intensity and long ISI conditions. A delay in P1 latency was also found by Williams et al. (1962, 1964) and Weitzman and Kremen (1965). Kevanishvili and Specht (1979) also reported a delay which, however, was much larger than in any of these studies. On the other hand, lowering the intensity and increasing the ISI did not produce any changes in P1 latency within wakefulness nor were any changes found within sleep. The removal of the slow wave from the sleep wave form may account for the differences in latency between wakefulness and the different stages of sleep. The slow wave may "pull" P1 closer to baseline levels in wakefulness thereby making it more difficult to identify P1. If components are defined as maximum peaks appearing with certain time periods, this approach may be subject to considerable error measurement.

During wakefulness, P1 was at or near baseline level. Erwin and Buchwald (in press) have recently reported that P1 decreases in amplitude with faster rates of stimulus presentation. The change from a slow to a fast rate of presentation did not have a similar effect in our waking subjects. Two reasons are offered for the discrepancies between studies. Our range of rates of presentation were limited compared to those employed by Erwin and Buchwald. Moreover, our fastest rate (1/1.1 sec) was comparable to one of their slowest. Differences in the low frequency filter setting (0.3 Hz in the present study versus 1 Hz for Erwin and Buchwald) could

also account for the P1 discrepancies. As mentioned, P1 is overlapped by the slow wNd wave. It was larger in the long than the short ISI condition. Therefore, wNd probably summed to P1 "pulling it" toward baseline, particularly for the long compared to the short ISI condition. The 1 Hz low frequency setting used by Erwin and Buchwald may well have attenuated the wNd slow wave, removing its overlapping influences. In our sleeping subjects, the overlapping influences were removed naturally. The experimental manipulation of the rate of stimulus presentation replicated those observed by Erwin and Buchwald.

During sleep, the amplitude of P1 was augmented significantly compared to wakefulness. This effect was consistent across all stimulus parameters. Osterhammel et al. (1985) and Erwin and Buchwald (1986) have however indicated that P1 decreases in amplitude within sleep and may disappear altogether in NREM. (In the case of Osterhammel et al., the component was identified as a mid-latency "Pb", but its 60-75 msec peak latency qualifies it as a probable "P1"). Again, methodological differences may account for the discrepant findings. The low frequency filter setting employed by Osterhammel et al. (20 Hz) and Erwin and Buchwald (10 Hz) was higher than what is typically used to record the late components. As mentioned in the previous paragraph, it is quite possible that these filter settings effectively removed a slow wave that overlaps P1 in the waking subject. However, this cannot explain why Erwin and Buchwald (1986) observed a complete removal of P1 in NREM whereas it was augmented in the present study. The three studies

differ in another important aspect. Osterhammel et al. and Erwin and Buchwald employed short duration stimuli (4 msec tones pips and clicks, respectively) as opposed to our 50 msec tones pips. The effects of stimulus duration on sleeping wave forms has not been systematically studies.

The amplitude of P1 returned to pre-sleep levels once the subjects were awakened in the morning. This suggests that the P1 augmentation was a true effect of sleep and not a confound of time-of-night.

The mean amplitude of P1 at Fz, Cz and Pz in wakefulness was approximately equal. During sleep, P1 was largest at Fz and Cz with the Pz amplitude consistently being smaller in all stages of sleep. Although these differences were not statistically significant, they were found in all conditions. We know of no other study which has examined the scalp topography of the late auditory evoked potentials in sleep. The differences in the waking and sleeping scalp topographies can be explained by an overlapping slow wave during wakefulness "pulling up" P1 frontally and centrally where it (the slow wave) was largest. P1 was unaffected by manipulation of stimulus intensity, either during wakefulness or in sleep. Although P1 was not affected by the rate of stimulus presentation during wakefulness, changes in its amplitude were seen in NREM sleep and to a lesser extent in REM. The differences between waking and sleeping suggest that P1 is at least partially endogenous in nature, although this endogenous nature can be explained by the overlapping slow wave. The fact that the rate of stimulus presentation had a

significant influence within sleep however qualifies it as an exogenous component. P1 therefore appears to be a fronto-centrally distributed component that manifests at least some of the characteristics of an exogenous component. These exogenous characteristics may however be compromised or masked by an endogenous slow wave as the subject becomes more conscious of the evoking stimulus.

The N1 Component

During wakefulness, the peak latency of N1b did not vary as a function of stimulus intensity. It was however prolonged when the rate of stimulus presentation was slowed from 1/1.1 sec to 1/3.3 sec. N1 seen in sleep was from 7 to 18 msec later than during wakefulness, regardless of stimulus intensity, rate or ear of presentation. These results are similar to a delay reported by Kevanishvili and Specht (1979) except that in their study N1 was prolonged by 15 to 65 msec. Most other sleep studies have observed either minimal (Osterhammel et al., 1973) or no change (William et al., 1962; Weitzman and Kremen, 1965; Ornitz et al., 1967a) in N1 latency. When subjects were awakened in the morning and subsequently tested, the peak latency of N1 was found to equal the pre-sleep latency. The prolongation of P1 latency was therefore continued into the N1 period. If auditory information is processed in a serial manner, it is quite possible that a delay in P1 latency will "carry over" to later N1 and P2 components. Again, as was the case for P1, it is also possible that the removal of an overlapping wNd within sleep gave the appearance of a prolongation of the

exogenous N1.

The most pronounced effects observed in this study were found to occur to N1 amplitude. The decrease in amplitude from wakefulness to sleep was highly significant and was consistent across all conditions. During NREM sleep, its amplitude was reduced to the extent that it was frequently recorded below baseline. During REM sleep, N1 occupied an intermediate position between that observed in wakefulness and NREM. This was also consistent across all five experimental conditions, although in some, the REM-NREM or REM-wakefulness difference did not reach significance. In the standard condition, N1 observed in early stage 2 also occupied an intermediate position. This was not observed in SWS (typically also occurring in the first half of the night) or in stage 2 recorded in the second half of the night. Upon re-examination of the early stage 2 data of individual subjects, it was found that the N1 recorded within the first half hour of sleep tended to be augmented compared to that recorded after an hour or more of sleep. When these very early stage 2 data are removed from the analysis, N1 appears to resemble that recorded in SWS (i.e. at or below baseline level). Noldy et al. (in press) systematically monitored N1-P2 during sleep onset. They also noted that N1 tended to be above baseline during the transition from wakefulness to stage 1 and to remain above baseline during the transition into stage 2. In all other conditions in the present study, when testing took place in early stage 2, N1 was always at or below baseline. Early stage 2 data therefore appear to be much closer to either

those seen in SWS or later stage 2 than in REM. In the morning, after subjects had been awakened, N1 was attenuated from the previous evening's level. This is likely a reflection that the subject's may not have been entirely alert. In certain cases, the EEG showed signs of stage 1 sleep.

The decrease in N1 amplitude is consistent with Williams et al. (1962) who used a baseline-to-peak measure, the baseline being established at stimulus onset. An examination of the illustration provided in their study indicates that the largest decrease in N1 occurred in SWS when it fell slightly below baseline. The amplitude in REM fell between the waking and NREM amplitudes. Fruhstorfer and Bergstrom (1969) also indicated that N1 is attenuated in NREM sleep. They did not record during REM sleep. The estimated (from the figures provided in their article) N1 amplitude in wakefulness and sleep were larger than that observed in the present study. This was likely due to their longer ISI (8 to 12 sec). Their sleep N1 was above baseline (i.e: negative amplitude) again in contrast to the present findings. Fruhstorfer and Bergstrom tested their subjects during an afternoon nap. Their findings may therefore be related to our very early stage 2 data.

The large decrease in N1 amplitude can also explain why studies which employed peak-to-peak measures (P1-N1, N1-P2) have also found a reduction in amplitude with sleep onset (Weitzman and Kremen, 1965; Anch, 1977; Kevanishvili and Specht, 1979). In this study, both P1 and P2 were often larger (i.e. more positive) in sleep than in wakefulness. The increase in P1 and P2 amplitudes was offset by

a larger decrease in N1. Consequently, peak-to-peak measures would be smaller in sleep than wakefulness.

A major assumption of this thesis was that the recording of evoked potentials during sleep provides a method to remove endogenous influences that often overlap the waking wave form. The massive drop in N1b amplitude in NREM sleep therefore suggests a novel and radical interpretation of the functional significance of this component. In the waking state, N1b is largely, if not entirely, endogenous due to the overlapping effects of a wNd wave. Manipulations of the physical stimulus therefore must produce changes in N1b amplitude because of their psychological consequences. As the intensity of the stimulus is increased or the interval between stimulus presentations slowed, subjects will increasingly be unable to ignore them, whether instructed to do so or not. In REM sleep, the N1 data suggest that information is processed to a greater extent and for a longer period of time than in NREM. Again, this is consistent with the behavioural literature (Price and Kremen, 1980).

The classification of a component as "exogenous" or "endogenous" is dependent on a number of criteria (Donchin et al., 1978). An exogenous component is affected by manipulations of the physical stimulus. An endogenous component is not. The morphology of an endogenous component is constant regardless of the modality of stimulus presentation. By comparison, the scalp topography of an exogenous component is highly dependent on the modality of the eliciting stimulus, while the scalp topography of an endogenous

component is invariant. To be classified as an endogenous component, N1b must fit these criteria. There are a number of problematic areas.

During wakefulness, N1b was affected by the physical manipulations of the stimulus. As mentioned, it was suggested that this could be explained in terms of the subject being unable to ignore the stimulus. Within NREM sleep, a period in which only an exogenous N1 remained, physical manipulations of the stimulus had unusual effects. Decreasing stimulus intensity had only a small effect on N1, and then only in SWS. Campbell et al. (in press) noted that N1 in SWS grew gradually in amplitude as stimulus intensity was increased from 60 to 100 dB SPL in 10 dB steps. There were no differences in stage 2 sleep. The alterations of N1 amplitude with variations in stimulus intensity are however much smaller than those observed during wakefulness. Anch (1977) reported that increasing stimulus intensity elicited a larger P1-N1 peak-to-peak amplitude in both wakefulness and sleep. It is, however, not clear whether this was due to a change in P1, N1 or both components. Increasing the ISI in the present study had the unusual effect of causing a decrease in N1 amplitude during NREM sleep. An investigation of individual subjects indicated that this NREM effect was consistent in both stage 2 and SWS. Since the response characteristics of the NREM N1 are different from those of the waking N1, they must reflect different modes of cerebral processing between the two states.

Additional evidence of the differences between the sleeping

and waking N1 is derived from their respective scalp topographies. The interactions between stage of sleep and electrode location indicated that the distribution of N1 in NREM sleep was more posterior than the fronto-central N1 recorded in wakefulness and REM sleep. We know of no other study that has examined the scalp topography of N1 in sleep. Different scalp topographies are indicative of different intra-cerebral generators (Picton and Stuss, 1980). The waking N1, largely endogenous in nature due to an overlapping wNd, would accordingly be generated at a different site than the sleeping N1. It is of course possible that at least two generators are active in the latency range of N1 during wakefulness, while only one of these remain active in sleep.

N1-like wave forms have also been observed to vary with manipulation of the subject's level of attention in both the visual and somatosensory modalities. In the visual modality, a broad negative parietal-occipital component in the 150 to 300 msec range may be altered by focusing attention on the eliciting stimulus (Eason, Harte and White, 1969; Harter, Aine and Schoeder, 1982; Hillyard, Munte and Neville, 1985; Hillyard and Munte, 1984). This visual negativity is maximum over the parieto-occipital areas of the scalp. In the somatosensory modality, manipulation of the subject's level of attention has been demonstrated to affect a negative component beginning at around 75 msec and peaking at 140 msec (Desmedt and Robertson, 1977). A variety of late components of the somatosensory evoked potential are also attenuated in sleep, including N140 (Desmedt, Brunko and Debecker, 1980). The

somatosensory N140 is largest over somatosensory cortical areas contralateral to the attended stimuli. The scalp topographies of the auditory N1 (or Nd), visual N150-350 and somatosensory N140 are thus quite different. Both the visual and somatosensory late negativities are largest over primary cortices. The auditory N1-Nd is not largest over the temporal regions, site of the primary auditory cortex. It is maximum over fronto-central areas of the scalp.

The location of the generators of N1 (or Nd in waking subjects) has not been established. There are a growing number of studies that offer support for the notion of multiple generators within the auditory N1 latency range. Hansen and Hillyard (1980, 1983) have noted that the early portion of their Nd had a frontal-central distribution very much like that of the N1 recorded to unattended stimuli. Its frontal distribution and its functional role in attention suggest N1 may be generated in the frontal lobes. However, patients with unilateral frontal lobes show no evidence of abnormal asymmetrical N1s (Knight, Hillyard, Woods, and Neville, 1980). Several studies have suggested that N1b might in fact be generated in the temporal area. A number of laboratories have reported a polarity inversion of an N1-like wave in temporal regions but the possibility of activity in the reference electrode makes its interpretation difficult (Vaughan and Ritter, 1970; Kooi, Topton and Marshall, 1971; Wolpaw and Wood, 1982). Mathematical modelling of the N1 coronal scalp distribution has also identified bilateral dipole sources in the temporal lobe (Peronnet et al., 1984; Scherg

and Cramon, 1985). Recently Scherg et al. (1986) have identified two possible dipoles within the temporal lobes. The first "N100t-P180t" appeared to be oriented tangentially (vertically) and resembled the classical vertex potential or N1b-P2. The second was associated with a more variable wave form, "P100r-N150r" and could be described by a radially (horizontally) oriented dipole. This may correspond to the N1c potential observed in the present study. Neuromagnetic recordings (Hari et al., 1980) have also pointed to a possible temporal N1b generator. Reports from patients with temporal lobe lesions are however inconsistent. Some have noted a complete absence of N1-P2 (Jerger, Weibers, Sharbrough and Jerger, 1969; Michel, Peronnet and Schott, 1980) while others have noted a completely normal response (Parving, Salomon, Elberling, Larsen and Lassen, 1980; Woods et al., 1984). The Scherg et al. (1986) study offers an explanation of these controversies. Their late auditory evoked potentials (N100t-P180t) and (P100r-N150r) in patients with lesions of the primary auditory cortex (areas AI, AII and AIII) and the distal portion of the acoustic radiation were significantly reduced or absent over the damaged hemisphere. In patients in whom only the acoustic radiations were damaged, the wave forms were delayed but its amplitude was preserved.

N1b was near or below baseline levels across all conditions in NREM sleep. Scherg et al. (1986) also reported a nearly complete removal of N1b in patients with lesions of the primary auditory cortex. Cerebral blood flow studies have also indicated that auditory association areas and mid-temporal cortex are very active

when subjects are attending to auditory tasks. Furthermore, single unit recordings from monkeys engaged in an auditory selective attention task also suggest a role for the primary auditory cortex (Benson and Heinz, 1978). It is therefore possible that the reduction of N1b amplitude in sleep may be a result of inactivity in the primary auditory cortex.

There appears to be some evidence that in spite of its fronto-central topography, N1b is generated in the primary auditory cortex. Similarly, visual and somatosensory endogenous negativities also appear to be generated in their respective primary cortices. Thus although the different N1-like wave forms have different scalp topographies, they seem to share functional significance (related to the subject's level of attention) and a common generation at or near the site of the primary cortex. Desmedt, Debecker and Robertson (1979) proposed that these attentional-related negativities may index modality-specific focal processors responsible for early stimulus identification.

The N1 observed in the sleeping subject had a posterior scalp topography unlike the frontal-central topography observed of the N1 in the waking subject. As already mentioned, the sleeping N1 was affected in a rather unusual manner by manipulations of the physical stimulus. Very little is known about this N1. Given its posterior scalp topography it is possible that it too is generated in the temporal lobe. Its latency was approximately 10-15 msec later than the N1-wNd. It therefore overlaps the latency range of N1c. N1c, like N1b, was markedly attenuated within sleep,

regardless of the ear of stimulus presentation. This was also the case of the earlier N1a. Therefore, N1a,b and c all appear to be largely endogenous in nature. Given their similar latency range and functional significance it is not clear whether the sleeping N1 and N1c are, in fact, separate processes.

The P2 Component

The P2 component showed the least amount of change of the late components from wakefulness to sleep. In the standard condition, its latency remained constant across the different levels of arousal. This corroborates similar results found by Williams et al. (1962) and Weitzman and Kremen (1965). In contrast, Kevanishvili and Specht (1979) reported delays of 15 to 45 msec while Fruhstorfer and Bergstrom (1969) found the sleep P2 occurred slightly earlier than the waking P2. Kevanishvili and Specht however employed a loudspeaker for stimulus transduction. It is thus possible that the apparent P2 latency shift might be an artifact of subject movement altering the position of the ear relative to the loudspeaker. It is not clear why the sleep P2 occurred earlier than the waking P2 in the study by Fruhstorfer and Bergstrom but this effect has not been replicated.

Both P1 and N1 were delayed from 10 to 20 msec within sleep. These consistent latency shifts suggest that information is processed in a serial manner. It therefore would have been expected that P2 would have also been prolonged by this extent. It was not. An alternative explanation of the P1 and N1 effect was that in wakefulness, they were overlapped by wNd. This endogenous wave form

summed to P1 and N1 and to a much lesser extent with P2. A by-product of this summation within the waking subject might be that P1 and N1 appear to peak at an earlier latency than the sleeping, exogenous components. The waking P2, relatively less affected by the overlapping effects of wNd, would be maximum in amplitude at a latency that is more or less constant during wakefulness and sleep.

The amplitude of P2 was, in general, larger (more positive) in sleep than in wakefulness. This approached statistical significance in the standard condition with the largest differences from the waking P2 being found in early stage 2 and REM. Only slight differences were found in SWS and late stage 2 compared to wakefulness. The data recorded for P2 across the stages of sleep in the standard condition were more variable than in the low intensity and long ISI conditions. When stimuli were presented monaurally to the left or right ear, P2 amplitude appeared to be invariant in those few subjects recorded in REM and NREM. The variability of P2 in the standard condition was therefore not representative of other conditions in this study. P2 is therefore well-preserved within sleep unlike the case for N1. Unfortunately, the functional significance and intra-cerebral generators of P2 are poorly understood. In the patients in whom Scherg and Von Cramon (1986) observed a complete absence of N100t ("N1b"), P180 ("P2") was also not apparent in their illustrations (although actual data were not presented). The apparent contradiction between the Scherg and Von Cramon findings (P2 absent when N1b is also absent) and the present findings (P2 normal in spite of the absence of N1b) is not easily

explained. It is possible that the generation of P2 requires that the primary auditory cortex be intact although not necessarily completely active. Williams et al. (1962) reported an opposite P2 effect to that observed here. Stimuli were presented via a loudspeaker and as already discussed, constancy of auditory input could not be assured within sleep due to possible changes in body position. All late components in their study were found to be reduced in amplitude suggesting an attenuation of auditory input to the sleeping subject.

Experimental manipulation of the physical characteristics of the stimulus had a similar effect on P2 amplitude in sleep and wakefulness. P2 was larger (more positive) following presentation of the high compared to the low intensity stimulus. Unlike Buchsbaum et al. (1975) who noted an increase in the "mean amplitude" (see Chapter 1 - Introduction) of P2 in only stages 3 and 4, the present study found that this relationship was constant across wakefulness and in all stages of sleep. Campbell et al. (in press) also noted that the P2-stimulus intensity relationship was consistent during wakefulness and within NREM and REM stages of sleep. A significant interaction was found between the level of arousal and the effects of the rate of stimulus presentation. When a fast rate of presentation (1/1.1 sec) was employed, P2 was invariant across wakefulness, NREM and REM sleep. When it was slowed to 1/3.3 sec, P2 was significantly larger in NREM sleep than in either REM sleep or wakefulness. This interaction must be considered with caution. Three subjects were excluded from the

analysis since they were missing REM data in the long ISI condition.

This increased the amplitude of the waking P2 in the short ISI (i.e. standard) condition compared to that found when these subjects are included in the grand average (compare Tables 2.2 and 2.4). No changes occurred in the NREM and REM grand averages. A reexamination of the data in the long ISI condition indicated the amplitude of P2 was somewhat smaller (about 2 uV) in wakefulness and NREM when these subjects were included in the grand average. In effect, the amplitude of P2 appeared to increase in NREM sleep relative to wakefulness in both short and long ISI conditions when these subjects were included in the grand averages.

The scalp topography of P2 did not vary between the different levels of arousal. It was largest at Cz with Fz and Pz being approximately of equal amplitude. Since the experimental manipulations produced similar effects of P2 in wakefulness and sleep as well as the fact that the scalp distributions were similar in the two states suggests the waking and sleep P2 components reflect the same processes. P2 was however somewhat attenuated during wakefulness. This was again probably due to the overlapping endogenous effects of the wNd wave. Nevertheless P2 was much less affected than either P1 or N2. It is therefore largely exogenous in nature.

The N2 Component

There were large differences in the N2 component between wakefulness and sleep. An increase in latency was found in all stages of sleep such that the NREM N2 appeared 40 to 50 msec later

than in wakefulness. N2 was also observed in REM sleep but it fell between the waking and NREM values. The latency of the waking and sleeping N2 did not change with changes in intensity or ISI. The amplitude of the sleep N2 was larger in NREM and REM sleep than in wakefulness in all conditions. The REM N2 was however reduced in amplitude compared to that seen in NREM. The large increase in the N2 component from wakefulness to sleep has been well established in most studies (Williams et al., 1962; Weitzman and Kremen, 1965; Fruhstorfer and Bergstrom, 1969; Ornitz et al., 1967a; Kevanishvili and Specht, 1979).

N2 was significantly larger for the higher than the lower intensity stimuli in wakefulness and sleep. Similarly, it was larger when a slow rate of presentation was employed, although the difference did not reach significance. There were no statistical differences in the scalp topography of N2 across the different stages of arousal. It had a fronto-central distribution with a maximum amplitude at Cz.

A variety of late N2s have been reported in the literature. In the waking state, the N2 observed in this study resembles Naatanen's (in press) "basic N2", as opposed to his "target N2" (or N2b) or the Mismatch Negativity ("N2a") observed in signal detection tasks. A late "N400" has also been observed in adults in tasks involving semantic incongruity (Kutas and Hillyard, 1980) or in naming tasks (Stuss, Cerri and Picton, 1983). Children display an unusually large negativity at about 400 msec when very novel, unexpected stimuli, such as an abstract painting are presented or when they are

asked to discriminate between two line drawings (Kok, 1985).

Whether the sleep N2 is a reflection of any of these late waking negativities is unknown. It would appear that it (the sleep N2) forms part of the K-Complex (Ujjaszi and Halasz, 1986). This would explain why it is larger in NREM than REM. K-Complexes are more frequent following high intensity tone pips, presented at slow rates (Campbell et al., 1985). The apparent increase in N2 amplitude in similar experimental situations may be an artifact of the averaging process. For example, the N2 will be larger when trials containing the high amplitude K-Complex are averaged than when only trial that have none are averaged. The prolonged latency (350-500 msec) of these late waves suggest that the stimulus has already received a considerable amount of processing. Common to these negative waves is the implication of some sort of memory search, whether short- or long-term. The amplitude of the sleeping N2 may be a manifestation of the degree of memory search. Following stimulus presentation, a "dictionary" of highly relevant information may be searched automatically. If a match is found, sleep may be "interrupted". N2 would therefore reflect an arousal process. On the other hand, it could be argued that this automatic memory search provides a means of inhibiting arousal from sleep when the incoming stimulus fails to match any of the "dictionary units".

Table 2.1

Average Latency at Cz of
the Late Auditory Components In the Standard Condition
(Standard Error enclosed in parentheses)

Peak	Awake (night)	2 Early	SWS	2 Late	REM	Awake (morning)
=====						
Latency (msec)						
P1	46 (04)	51 (06)	68 (01)	60 (03)	61 (03)	49 (06)
N1	100 (03)	116 (05)	108 (05)	107 (06)	118 (06)	102 (07)
P2	197 (09)	196 (06)	198 (05)	189 (08)	201 (12)	198 (15)
N2	292 (13)	331 (05)	345 (10)	335 (18)	309 (09)	345 (13)

Table 2.2

Average Amplitude of the Late Auditory Components
Across Electrode Sites
in the Standard Condition
(Standard Error enclosed in parentheses)

Peak	Electrode	Awake (night)	2 Early	SWS	2 Late	REM
P1	Fz	0.97 (0.50)	2.22 (0.63)	2.00 (0.86)	2.47 (0.92)	2.61 (0.72)
	Cz	1.04 (0.52)	2.19 (0.66)	2.01 (0.75)	2.32 (0.69)	2.63 (0.34)
	Pz	0.93 (0.65)	0.52 (0.62)	0.06 (0.65)	1.10 (0.69)	1.67 (0.34)
N1	Fz	-5.01 (0.76)	-1.98 (0.90)	1.11 (0.73)	1.25 (0.86)	-1.94 (1.29)
	Cz	-5.67 (0.94)	-2.42 (0.82)	0.69 (0.59)	0.76 (0.82)	-2.11 (1.52)
	Pz	-3.39 (0.54)	-0.92 (0.70)	-0.44 (0.69)	0.57 (0.66)	-0.29 (1.01)
P2	Fz	1.75 (1.22)	5.64 (2.32)	3.09 (1.42)	2.60 (1.29)	4.66 (1.37)
	Cz	3.56 (1.60)	7.62 (2.98)	3.94 (1.25)	4.10 (2.03)	5.94 (1.74)
	Pz	1.87 (0.82)	5.59 (2.17)	3.04 (0.70)	3.71 (1.89)	3.77 (0.94)
N2	Fz	-2.22 (0.82)	-7.56 (1.03)	-5.76 (2.31)	-4.05 (1.20)	-2.98 (1.28)
	Cz	-2.64 (0.99)	-10.47 (2.35)	-7.76 (4.36)	-5.82 (1.61)	-3.33 (1.01)
	Pz	-1.04 (0.49)	-6.39 (2.10)	-5.93 (1.77)	-4.05 (1.33)	-2.75 (1.16)

Table 2.3

Average Cz Latency and Amplitude of
the Late Auditory Components
in the Low and High Intensity Conditions
(Standard Error enclosed in parentheses)

		Latency (msec)		Amplitude (uV)	
		Awake (night)	NREM	Awake (night)	NREM
=====					
P1	Low	47 (04)	59 (04)	0.57 (0.22)	1.45 (0.49)
	High	46 (05)	59 (03)	1.17 (0.41)	2.25 (0.50)

N1	Low	100 (03)	109 (08)	-2.93 (0.27)	0.56 (0.44)
	High	99 (04)	111 (04)	-5.25 (0.51)	-0.44 (0.54)

P2	Low	177 (06)	199 (09)	2.21 (0.86)	4.06 (1.19)
	High	197 (10)	191 (05)	3.61 (1.14)	6.29 (1.58)

N2	Low	290 (13)	353 (12)	-2.15 (0.50)	-5.90 (1.86)
	High	296 (16)	331 (11)	-2.53 (0.79)	-7.05 (1.33)

Note: Data for the high intensity manipulation were derived from the standard condition and collapsed across early stage 2, SES and late stage 2.

Table 2.4

Mean Latency and Amplitude of the
Late Auditory Components at Cz
in the Long and Short ISI Conditions
(Standard Error enclosed in parentheses)

		Latency (msec)			Amplitude (uV)		
		Awake (night)	NREM	NREM	Awake (night)	NREM	NREM
=====							
P1							
	Long	52 (04)	65 (03)	65 (02)	1.00 (0.96)	4.10 (0.65)	2.22 (0.39)
	Short	55 (05)	59 (02)	62 (02)	1.39 (0.40)	2.51 (0.51)	2.55 (0.52)

N1							
	Long	115 (04)	112 (03)	115 (04)	-11.95 (1.11)	1.99 (0.71)	-4.02 (0.83)
	Short	106 (4.0)	117 (5.3)	116 (5.2)	-6.11 (0.72)	0.02 (0.34)	-1.13 (0.57)

P2							
	Long	199 (07)	205 (05)	201 (05)	9.42 (0.77)	14.01 (1.73)	8.38 (1.18)
	Short	187 (05)	201 (04)	195 (05)	5.00 (1.19)	5.21 (0.82)	5.85 (1.32)

N2							
	Long	297 (06)	343 (10)	318 (14)	-4.41 (1.42)	-18.19 (3.42)	-6.01 (0.97)
	Short	303 (17)	347 (04)	314 (11)	-2.90 (0.84)	-7.31 (1.54)	-3.65 (0.77)

Note: Data for the short ISI manipulation were derived from the standard condition and collapsed across early stage 2, SES and late stage 2

Table 2.5
Mean Amplitudes of N1a, N1b and N1c
in Left and Right Ear Conditions
(Standard Error enclosed in parentheses)

Peak	Ear	Awake		NREM		REM	
		T3	T4	T3	T4	T3	T4
N1a	left	-1.19 (0.35)	-0.31 (0.38)	0.13 (0.36)	0.23 (0.30)	-0.01 (0.17)	0.29 (0.33)
	right	-1.34 (0.37)	-0.90 (0.39)	0.15 (0.18)	0.39 (0.22)	0.24 (0.13)	0.22 (0.11)
N1b	left	-0.61 (0.48)	0.03 (0.41)	-0.22 (0.46)	0.41 (0.19)	-0.08 (0.24)	0.31 (0.35)
	right	-0.96 (0.45)	-0.63 (0.48)	0.01 (0.39)	0.59 (0.31)	-0.12 (0.22)	-0.26 (0.31)
N1c	left	-0.32 (0.32)	-0.61 (0.44)	0.42 (0.31)	0.82 (0.24)	0.15 (0.17)	0.41 (0.33)
	right	-1.21 (0.26)	-0.57 (0.40)	0.59 (0.38)	0.92 (0.35)	0.16 (0.36)	-0.13 (0.25)

Figure Legend

Figure 2.1 Superimposed wave forms of individual subjects recorded in the standard condition. The data from 10 subjects are shown in the waking wave forms. Nine subjects are shown in early stage 2, late stage 2 and REM while six subjects are shown in SWs and wakefulness in the morning. Stimuli were 80 dB SPL, 1000 Hz tone pips with a duration of 50 msec (5 msec rise-fall times) presented binaurally at a rate of 1/1.1 sec. Averages were computed online while subjects were reading in wakefulness and in the different stages of sleep. Each individual wave form is the average of 200 stimuli. Negativity in this and all other figures is indicated by an upward deflection.

Figure 2.2 Grand average (upper) and subtraction (lower) wave forms obtained to repetitive stimuli in the standard condition. The difference wave forms were obtained by subtracting the wave form recorded in the corresponding stage of sleep from the waking wave form. The principle differences between wakefulness and sleep are seen as a large decrease in N1 amplitude and large increase in P2 and N2 amplitudes within non-REM sleep. The subtraction wave forms show the waking wave forms were more negative than the sleep wave forms beginning at about 50 msec and continuing for 200 to 300 msec.

Figure 2.3 Grand average (upper traces) and subtraction (lower traces) wave forms to the 50 dB SPL stimulus. Stimulus parameters

were identical to those in Figure 1 except that the intensity was decreased from 80 to 50 dB SPL. Data from early stage 2, SWS and late stage 2 were combined to form NREM since few subjects had complete data in all these stages. The REM wave forms were computed from the data of only three subjects. These data were not statistically analysed. The REM effects are however consistent with other condition. N1 amplitude again decreased in sleep with the larger decrease seen in NREM. The increase of N2 in sleep is seen in NREM. The negative shift found in wakefulness relative to sleep began soon after stimulus onset and continued for several hundred milliseconds. In NREM sleep, this shift began about 50 msec after stimulus onset whereas in REM it appeared to occur at approximately the same time or slightly after stimulus onset.

Figure 2.4 Grand average (upper traces) and difference (lower traces) wave forms obtained in the long ISI condition. Stimulus parameters were identical to those in Figure 1 except that the ISI was increased from 1.1 to 3.3 sec. Data from early stage 2, SWS and late stage 2 were combined to form NREM data. N1 amplitude was more positive in NREM and REM sleep than in wakefulness. The increase in N2 was not as large in REM as in NREM sleep. The negative shift in this condition was much larger than in the other condition and began 10 to 20 msec after stimulus onset.

Figure 2.5 Grand average (upper traces) and difference (lower traces) wave forms obtained when stimuli were delivered to the left

ear. Stimulus parameters were otherwise identical to those in the standard condition. This condition was presented to examine the temporal N1a and N1c components in wakefulness and sleep. In wakefulness N1a was most visible at T3 where it peaked somewhat earlier than the vertex N1b. N1c was most visible at T4 in wakefulness and peaked slightly later than the vertex N1b. Note the absence of these components in both NREM and REM sleep. Only N1b was elicited in these stages and it was much reduced in amplitude consistent with conditions. The negative shift shown in the subtraction wave forms began at about the time of P1.

Figure 2.6 Grand averages (upper traces) and subtraction (lower traces) wave forms obtained when stimuli were presented to the right ear. Stimuli were identical to those in the standard condition. N1a and N1c are clearly seen at T3 and T4 in wakefulness. As in the left ear condition, there was no sign of these components in sleep.

Figure 2.1

Superimposed individual wave forms of individual subjects
recorded in the standard condition

STANDARD CONDITION

Intensity=80 dB SPL; ISI=1100 ms; Ear=binaural

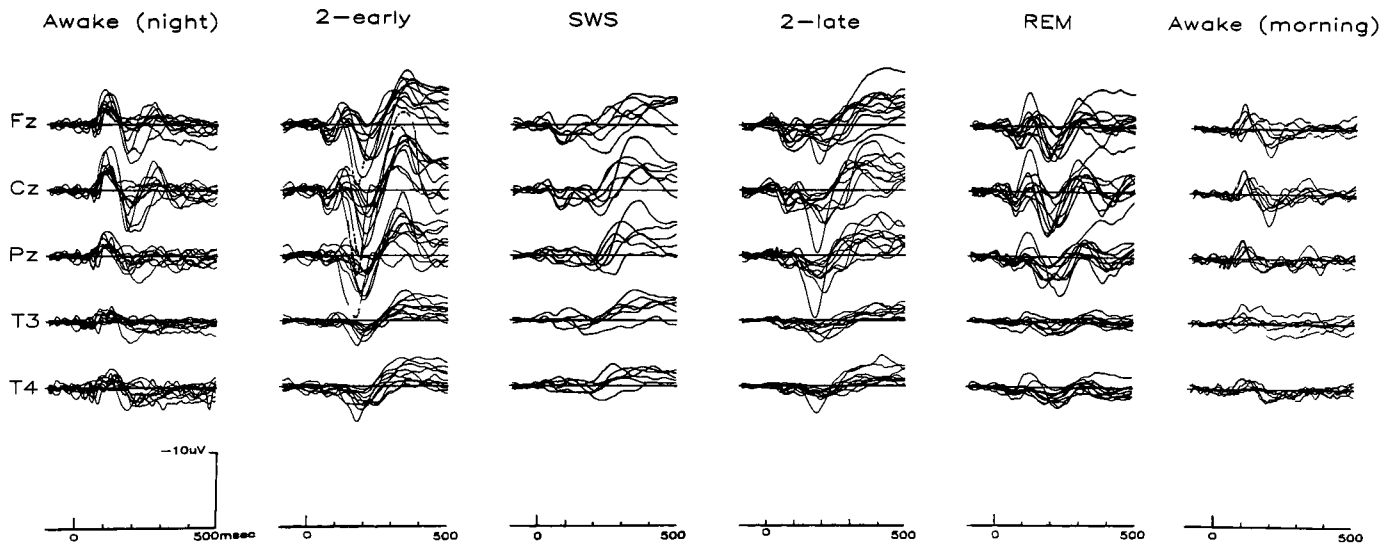


Figure 2.2

Grand average and subtraction wave forms in the standard condition

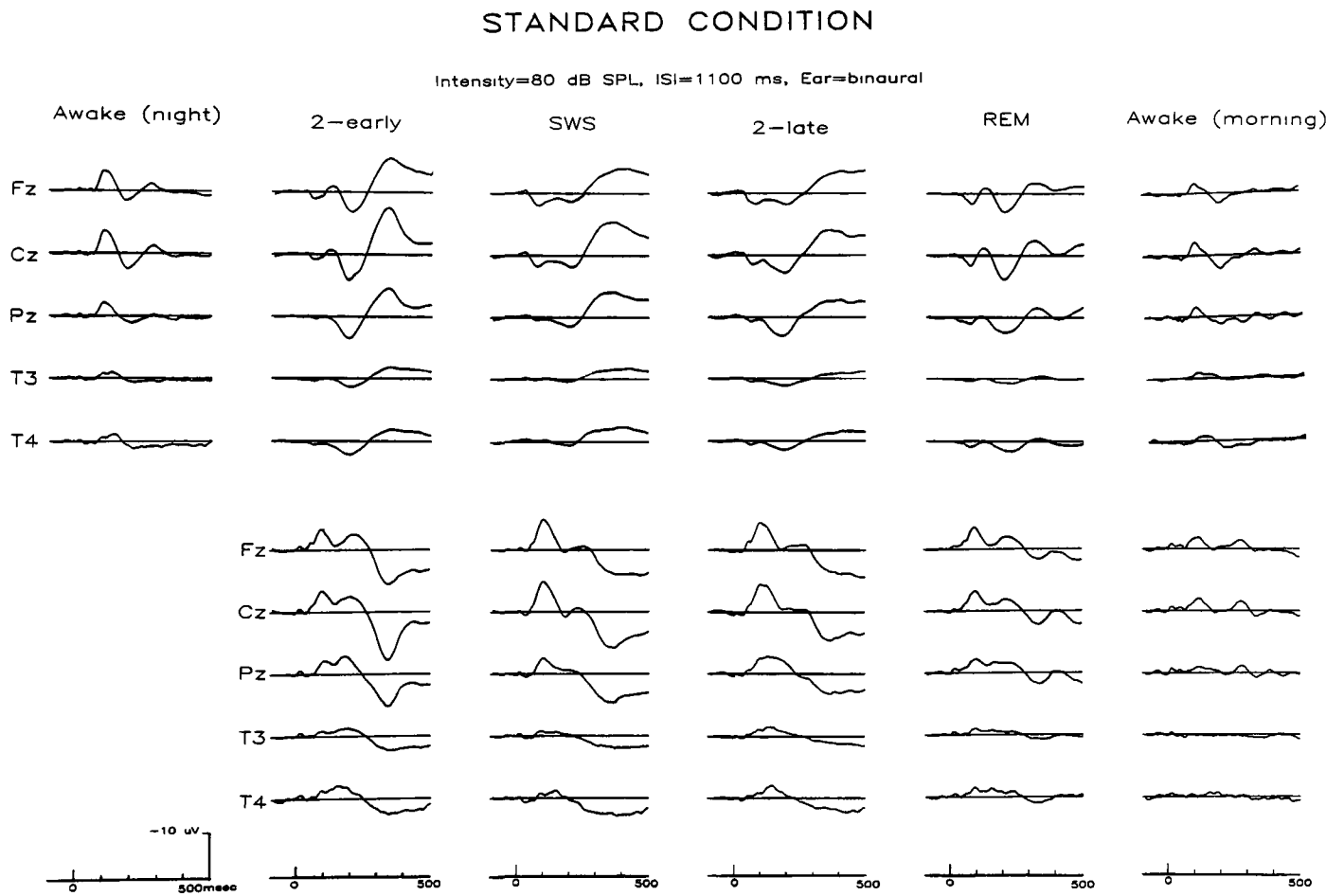


Figure 2.3

Grand average and subtraction wave forms in the
low intensity condition

LOW INTENSITY

Intensity=50 dB SPL; ISI=1100 ms; Ear=binaural

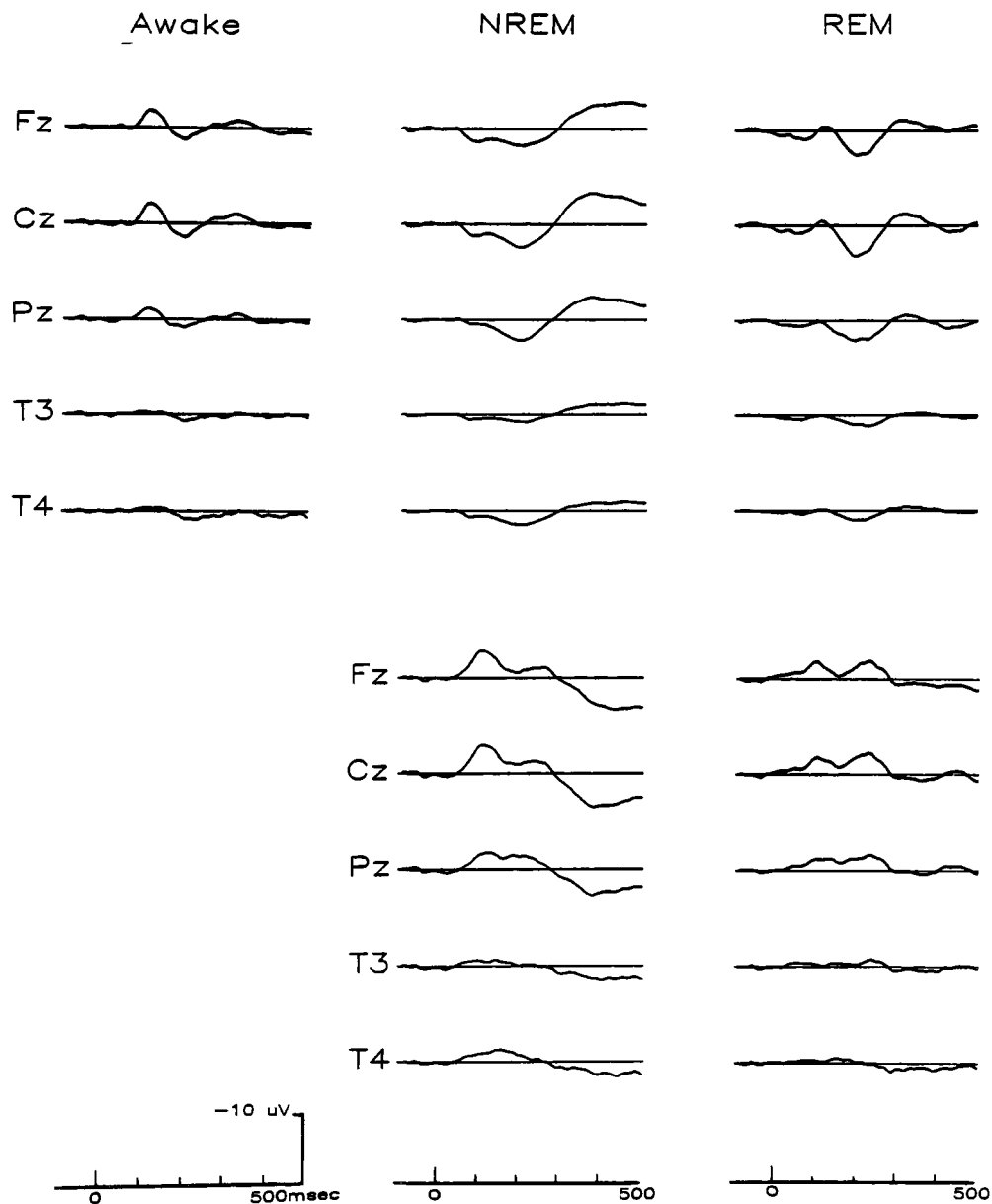


Figure 2.4

Grand average and subtraction wave forms in the
long ISI condition

LONG ISI CONDITION

Intensity=80 dB SPL; ISI=3300 ms; Ear=binaural

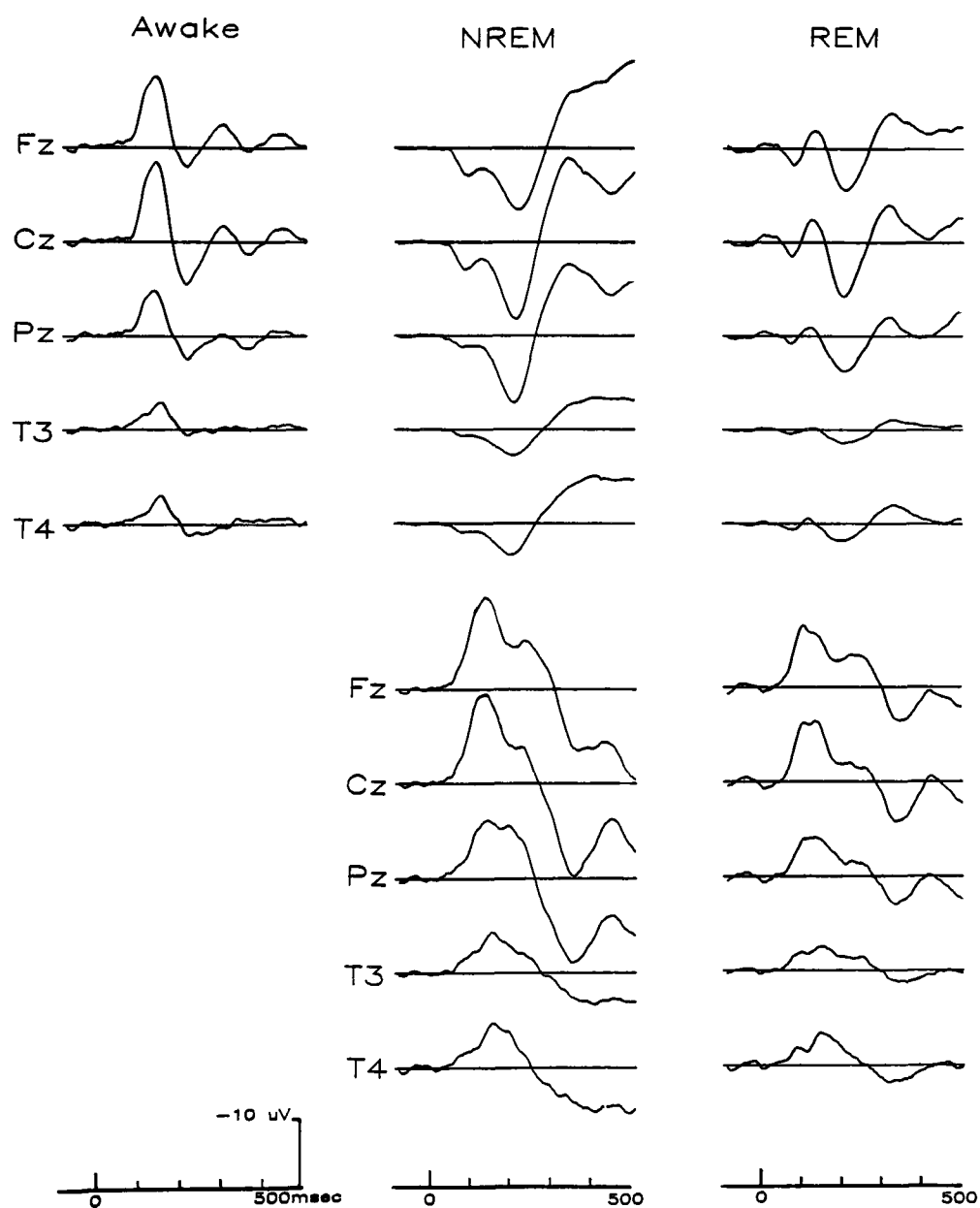


Figure 2.5

Grand average and subtraction wave forms in the
left ear condition

LEFT EAR CONDITION

Intensity=80 dB SPL; ISI=1100 ms; Ear=left

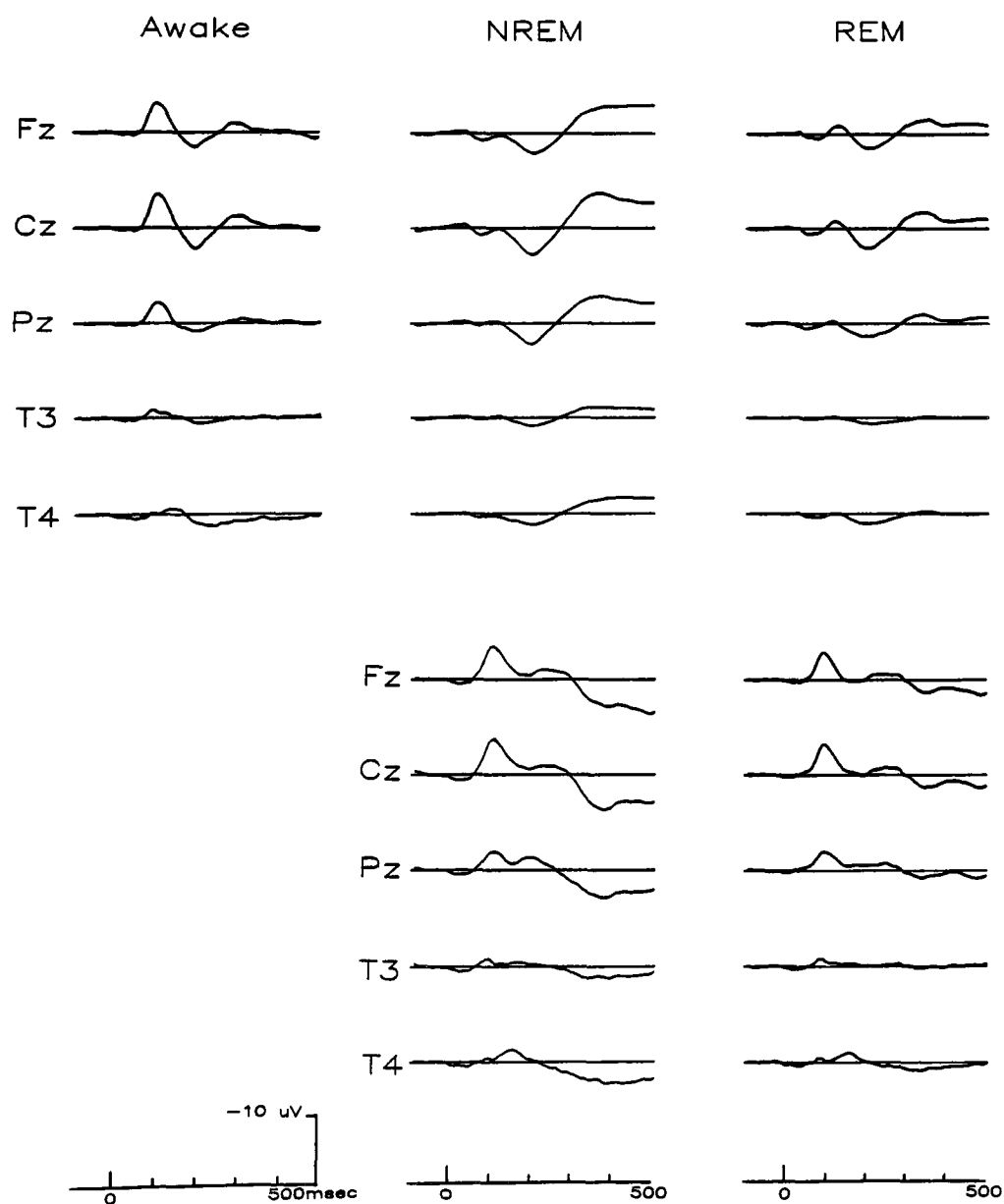
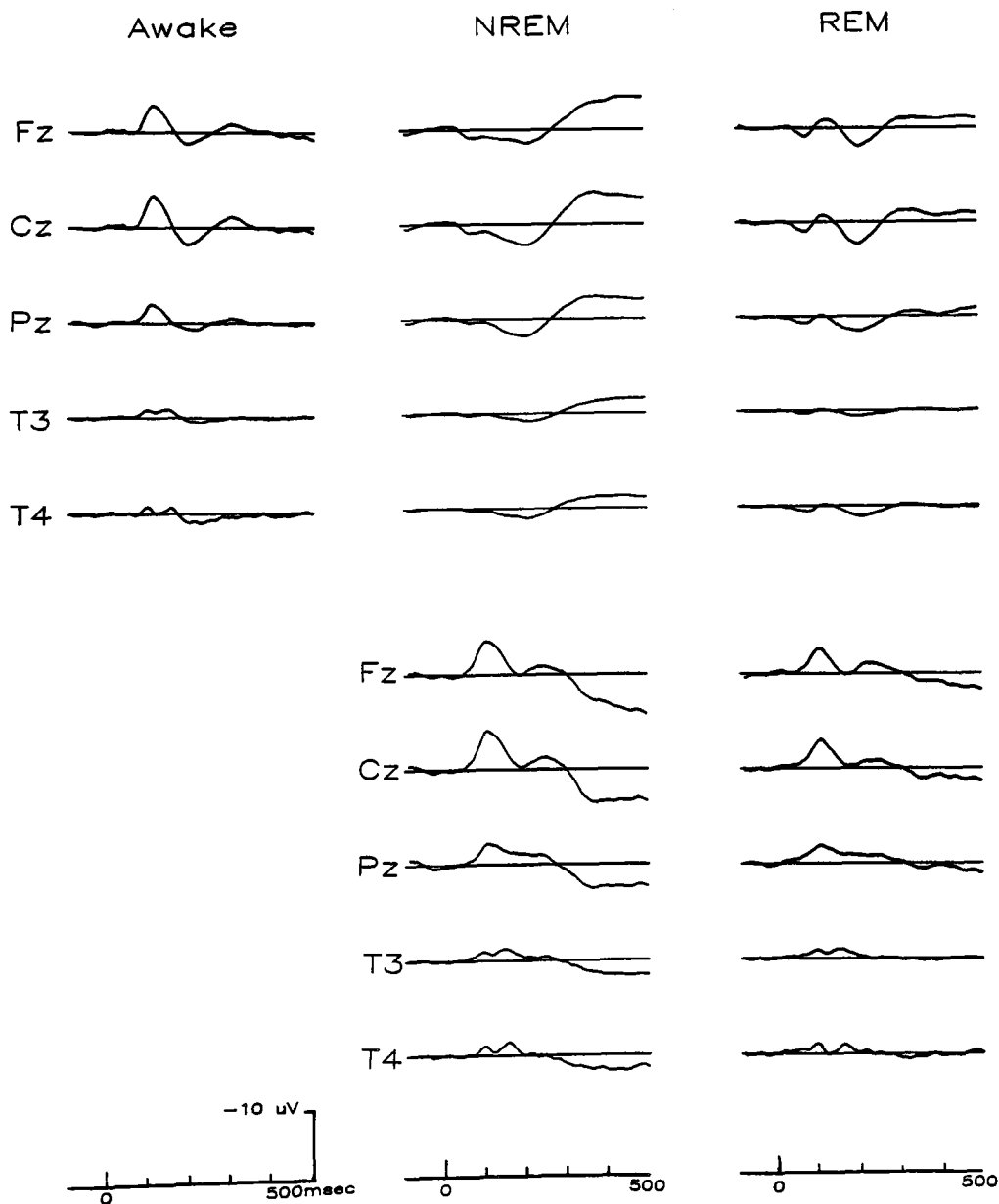


Figure 2.6

Grand average and subtraction wave forms in the
right ear condition

RIGHT EAR CONDITION

Intensity=80 dB SPL; ISI=1100 ms; Ear=right



Chapter 3

The Mismatch Negativity During Sleep

Introduction

The Mismatch Negativity (MMN) has been suggested to reflect an "automatic" comparative memory process which takes place regardless of the subject's attentional state. Naatanen and his colleagues have labelled the MMN as an exogenous component since it is elicited in the "odd ball" paradigm by deviant stimuli that are physically different from standard stimuli regardless of the subject's level of attention (Naatanen et al., 1978, 1980a, 1983; Sams et al., 1985b, 1986). Since it is probably not possible for the waking, conscious subject to ever completely ignore all stimuli, the MMN may in fact reflect attention-related processes. In an attempt to resolve this problem, sleep was used as an experimental manipulation to test the nature of the MMN. If processes reflected by the MMN are indeed exogenous, it should be elicited in the unconscious, sleeping subject.

The MMN has been reported to vary as a function of stimulus probability. In this study, deviant stimuli were delivered with probabilities of either .20 and .40. The lower probability deviant was expected to elicit a larger MMN than the higher probability deviant (Naatanen et al., 1983). Naatanen and Gaillard (1983) have also suggested the MMN will be larger as the physical difference

between the deviant and standard stimuli is increased. In another set of conditions, the frequency of the deviant stimulus was therefore made to vary from the standard stimulus (Sams et al., 1985b). Sams et al. (1986) were unable to elicit the MMN during stage 2 of sleep. In their study, standard stimuli were presented at a frequency of 1000 Hz while the deviant stimulus was presented at a frequency of 1050 Hz. The frequency difference between standard and deviant stimuli may have been too small to produce the MMN within sleep. Thus, in this study the deviant stimulus was presented in different conditions at a frequency of either 2000, 1250 or 1050 Hz while the standard stimulus which was maintained at a constant frequency of 1000 Hz. The widest frequency separation (1000 Hz) was expected to elicit a larger MMN than the middle frequency separation (250 Hz) which in turn was expected to elicit a larger MMN than the smallest frequency separation (50 Hz) (Sams et al., 1985b). As mentioned earlier, it is also possible that the failure to observe the MMN in the early portion of the night could be due to a low MMN signal-to-noise ratio. The optimal period for the recording of the MMN may therefore be in the second half of the night during either stages 2 or REM when delta activity is markedly lowered.

Methods

Subjects

Thirteen subjects (7 males and 6 females) between the ages of

19 and 36 volunteered to participate in this study. None reported having any hearing disabilities. They arrived 2 hours before their normal bedtime during which time electrodes were affixed and baseline testing took place. Not all conditions were run with all subjects, as will be explained in the procedure section. Subjects were told to refrain from ingesting coffee or alcoholic beverages or taking any drugs within a 24 hour period prior to testing. Three subjects had participated in EP research on two or more different occasions.

Procedure

In the "Standard" condition, 80 dB SPL tones having a duration of 55 msec (5 msec rise-fall times) were presented at a rate of 1/2 sec in each block of stimuli. Within a block of stimuli, 80% of the tones were presented at a frequency of 1000 Hz (standards) while the remaining 20% were presented at a frequency of 2000 Hz (deviants). The standard and deviant stimuli were presented in a random Bernoulli sequence. Although low deviant probabilities have been reported to produce larger MMNs, a large number of trials are required to obtain a sufficient number of deviants to obtain a high signal-to-noise ratio. During sleep stage changes are too frequent to permit long recording periods. The deviant stimulus was therefore presented at a probability of .20 in the standard condition to allow a sufficient number of responses to be averaged in the relatively short period of time that was available.

In the second, "High Probability" condition, standards were presented at a probability of .60 while deviant stimuli were

presented at a probability of .40. The intensity, frequency and rate of presentation of the standard and deviant stimuli remained identical to that employed in the standard condition. A third "Middle Frequency Separation" condition was also identical to the standard condition with the exception that the frequency of the deviant stimuli was changed to 1250 Hz. A sub-group of six subjects was also run a the fourth "Small Frequency Separation" condition in which the frequency of the deviant stimuli was set at 1050 Hz. In each condition, 100 stimuli were presented. The standard, middle and low frequency conditions were replicated three times while the subjects was awake and whenever possible during sleep. The high probability condition was replicated two times while the subject was awake and again, whenever possible during sleep. Pilot data run for the present study have indicated that the MMN could not be seen early in the night (in early stage 2 and SWS). For these reasons, only the standard condition was run consistently in early stage 2 and SWS. Other conditions were run in these stages whenever time permitted.

Testing took place in a sound attenuated sleep laboratory. In Attend conditions during wakefulness, subjects were instructed to count the number of deviant stimuli. As verification of attentiveness, the deviant count was checked at the end of each of block of stimuli. In Ignore conditions during wakefulness, subjects were instructed to read a book and ignore the auditory stimuli. The reading condition was designed to manipulate attentiveness away from the auditory stimuli while maintaining a high level of arousal. The

standard, middle and low frequency separation and high probability conditions were run under the Attend and Ignore manipulations. Once baseline testing was completed, the lights were turned off and subjects were allowed to fall asleep.

Stimuli were delivered by a specially designed (Starkey Laboratories Inc.) behind the ear hearing aid device. Speaker output from a Knowles ED-197 wide bandpass receiver was conducted through the earhook (about 5 cm long) of the hearing aid which in turn was connected to 4 cm of no. 13 standardized tubing (1.93 mm in diameter). Individually fitted ear moulds were attached to the end of the standardized tubing. This system was calibrated using a Bruel and Kjaer 2209 sound level meter and a 2 cc coupler. A 0.2 V RMS input signal produced a relatively flat response (94-100 dB SPL) from 100 to 4000 Hz. The ear mould was placed in the subject's ear of preference.

Physiological Recording

The electroencephalographic (EEG) and electro-oculogram (EOG) were recorded using Grass gold electrodes attached to the scalp with collodion- soaked gauze. Electrodes were placed at Fz, Cz, and Pz (10-20 system) and referenced to the mastoid opposite the ear of stimulation. EOG electrodes were placed superior to the canthus of the left eye and inferior to the canthus of the right eye. This permitted the monitoring of both horizontal and vertical eye movements on a single polygraphic channel. Interelectrode impedance was below 5 kOhms. The EEG and EOG were recorded using Nihon-Kohden EU/50 amplifiers with a high filter setting of 35 Hz and a time

constant of 0.3 sec. The physiological signals were also written out on paper at a speed of 10 cm/sec. The sleep EEG was scored online by an experienced rater as being either stage 2, 3, 4 or REM sleep. Standard Rechtschaffen and Kales (1968) scoring methods were employed. Stage 2 was divided into early and late halves. Stages 3 and 4 were combined to form slow wave sleep (SWS). Testing in sleep began after the subject had been in definite stage 2 or SWS for more than 5 minutes. In cases of stage ambiguity, the records were later scored by a second, experienced rater. If the two raters disagreed, the condition was rejected from further analysis. Signals were recorded using a 600 msec sweep time (2 msec dwell time). Online averaging began 100 ms prior to stimulus onset. It was discontinued when the EEG sleep pattern showed signs of a stage change or artifact (typically muscle artifact or movement). During wakefulness, trials in which either EEG (Fz) or EOG channels exceeded ± 75 μ V were rejected from the ongoing average. During non-REM (NREM) sleep, the artifact reject was set at ± 100 μ V to accomodate the high amplitude EEG in sleep. Such a system resulted in the rejection of trials "contaminated" by frontal K-complex often seen in NREM and eye movement artifact (horizontal or vertical) in REM. All averaged EP wave forms were stored on floppy disk for subsequent offline plotting and analysis.

Evoked Potential Analysis

Subtraction wave forms were computed by subtracting, point-by-point, the standard wave forms from the deviant wave forms at each electrode site recorded in the same condition. Analyses

were conducted only on data obtained from the subtraction wave forms. The 600 msec sweep period was sub-divided into nine 50 msec intervals beginning 50 msec after stimulus onset. These intervals were labelled according to the time at which they began. Hence, the 50-100 msec time period is referred to as the 50 msec interval, the 100-150 msec time period is referred to as the 100 msec interval and so on. Within each of these intervals, the average amplitude was computed. A similar scoring procedure has been employed by Naatanen and his colleagues (Naatanen et al., 1981; Sams et al., 1986). The actual determination of the existence of the MMN within sleep is not without its methodological difficulty. A simple approach would be to compare waking and sleeping difference wave forms. However the failure to find a significant difference between these wave forms cannot be used to imply the presence of a MMN in sleep.

In order to prove that the sleeping MMN did not differ from that observed in wakefulness, the following logic was applied:

1. The MMN was measured in a difference wave form. In any one interval, on a strictly random basis, the difference might be of a negative or positive polarity. The probability of occurrence of a negative-going deflection within wakefulness was therefore 1:2. The probability of occurrence of an MMN within wakefulness and sleep was therefore 1:4.

2. The MMN occurs within a specific 50 to 250 msec latency period. Hence only negative-going deflections occurring within the 50 to 200 msec sub-intervals were considered to be possible MMNs.

3. Confidence intervals were computed for each of these

possible MMNs. This procedure determined whether the probability that the mean value of a sub-interval fell within a particular upper and lower range. If the lower limit exceeded zero (i.e. was negative) the sub-interval was considered to contain a MMN. The procedure is equivalent to the computing of a t-test between the deviant and target wave forms (Winer, 1971, p.25). Because a negative directionality is predicted, a one-tailed test of significance ($p < .05$) was applied to the confidence intervals.

4. To further restrict the likelihood of chance findings, in order to be called an MMN, the scalp distribution of the negative deflection had to conform to that observed in the literature. Thus, frontal or central wave forms had to be of greater amplitude than the parietal wave form.

5. When a MMN was identified in wakefulness, a repeated measures ANOVA was run to compare its amplitude to the mean amplitude of sleeping wave forms within the identical interval.

6. It is possible that the MMN could occur at a different latency within sleep. Thus, the peak of a possible MMN observed in sleep (steps 3 and 4) was compared to the peak MMN in wakefulness, regardless of the interval in which they appeared.

Results

The data analysis during sleep was limited to late stage 2 and REM sleep. Pilot data obtained from early stage 2 and SWS were not analysed since the difference wave forms were clearly not representative of the MMN component. These difference waves

deviated in a positive direction from baseline in the 50 to 250 msec interval. Complete data from wakefulness, late stage 2 and REM sleep were only available for nine subjects in the standard condition, seven subjects in the high probability and middle frequency separation conditions and four subjects in the low frequency separation condition. Analyses comparing the reading, late stage 2 and REM data were only conducted on these subjects.

Standard Condition

The upper portion of Figure 3.1 shows the grand average wave forms recorded in the standard condition in wakefulness and in the various stages of sleep. Wave forms to deviant stimuli are represented by the thick lines while those to the standard stimuli are represented by the thin lines. The lower portion of this figure represents difference wave forms obtained by subtracting the standard from the deviant wave forms recorded in the same condition.

Standard stimuli in the reading and counting conditions elicited N1, P2 and N2 deflections. In wakefulness, N1 and N2 had a fronto-central distribution while P2 appeared to have a more central distribution. While deviant stimuli elicited similar N1 and P2 deflections, an N2-P3 complex elicited in the Attend ("Count") condition was not seen in wave forms in the Ignore ("Read") condition. A MMN was not visible in early stage 2 (7 subjects) or SWS (6 subjects). Indeed, if anything, a mismatch positivity was observed within the expected latency intervals.

----- Insert Figure 3.1 here -----

The mean amplitudes in each interval of the subtraction wave form are shown in Table 3.1. Negative values indicate the target wave form was more negative than the standard wave form whereas the reverse is true when the mean amplitude are positive. In the reading condition, the mean amplitudes were significantly different from zero at Fz and Cz in the 100 to 200 msec intervals. At Pz, this negativity was significant in the 150 and 200 msec intervals. Within the first 250 msec, the difference wave form tended to be most negative centrally, declining slightly frontally and much more so parietally. In the counting condition, a slow negative deflection was found in the subtraction wave forms which peaked within 100 to 150 msec of stimulus onset. This however did not reach statistical significance at any of the electrode sites. The amplitudes in these intervals were larger at Fz and Cz than Pz. Although the mean amplitudes in intervals from 200 msec to the end of the sweep were highly significant, they were probably a reflection of the N2b-P3 process rather than the MMN. As can be observed in Figure 3.1, in early stage 2 and SWS, no MMN was visible. In late stage 2 and REM sleep, none of the mean amplitudes in the 50 to 200 msec intervals attained significance. In fact, amplitudes in the 100 to 300 msec intervals were generally positive in both late stage 2 and REM sleep. The only significant deviations from baseline occurred at a later period during late stage 2 (Fz: 250 msec interval) and REM (Pz: 400 msec interval) when the deviant wave form was significantly more positive than the standard wave

form.

----- Insert Table 3.1 here -----

There were no statistical differences in the mean amplitudes in the reading condition and sleep stages 2 and REM.

Deviant Probability Condition

Grand average wave forms for the high probability condition are shown in the upper half of Figure 3.2. The subtraction wave forms (deviant minus standard) are shown in the lower half of Figure 3.2. The mean amplitude for the nine sub-intervals are given in Table 3.2. In the reading condition, the negativity was significant in the 50 and 100 msec intervals at both Fz and Cz. The negativity extended into later intervals but only reached significance in the 200 msec interval at Cz and Pz. A comparison of amplitudes among the electrodes indicated that the difference was larger at Fz and Cz than Pz. In the counting condition, the mean amplitudes were significantly more negative than baseline in the 50 msec interval at all electrodes. The negative-positive deflection (200-350 msec) observed in the difference wave forms corresponded to the N2b-P3 complex.

----- Insert Figure 3.2 and Table 3.2 here -----

During late stage 2 and REM sleep, large negative amplitudes were recorded in the 50 and 100 msec intervals. Statistical

differences were obtained in stage 2 at Pz (100 and 150 msec) and in REM at Fz and Cz (50 msec). The amplitudes in the later 150 to 250 msec intervals were mainly positive. The distribution was more fronto-central in the 50 msec interval but appeared to become more central in the 100 msec interval. The difference wave forms were somewhat more negative in sleep than wakefulness in the 50 and 100 msec intervals and reflected the early onset of the negativity in sleep relative to wakefulness. There was no significant differences in the amplitude of intervals containing a MMN in the reading conditions and the same intervals in late stage 2 or REM. Furthermore, there were no significant differences between the MMNs in the reading condition and those observed in sleep regardless of their latency.

Middle Frequency Separation Condition

Figure 3.3 represents the grand average and difference wave forms recorded in wakefulness and sleep. The mean amplitude for each interval of the subtraction wave forms is presented in Table 3.3. Although a protracted negativity was seen in the difference wave form recorded in the reading condition, statistical differences between the mean amplitudes and baseline were obtained only at Fz in the 250 msec interval and at Cz in the 50 msec interval. There was a nonsignificant tendency for this negativity to be larger at the frontal and central electrodes than parietal in the 50 to 150 msec interval. In the 200 msec interval, the amplitude at Fz was statistically larger than at Cz and Pz. In the counting wave forms, a well defined fronto-central negativity peaked at about 100 to 150

msec. However, the mean amplitude was significantly different from baseline only at Fz in the 50 and 100 msec intervals. As in previous conditions, the later negative-positive deflection beginning at 200-250 msec in the subtraction wave form corresponded to the N2b-P3 complex elicited by detected deviant stimuli.

----- Insert Figure 3.3 and Table 3.3 here -----

During late stage 2, the difference wave form was positive throughout the first 300 msec contrary to the expected morphology of the MMN. In REM sleep, a broad negativity was visible at Cz in the 100 to 200 msec latency period and to a lesser extent at Fz and Pz. It was not statistically greater than zero in any of these intervals. Even though a significant MMN could not be observed in sleep, the amplitude of the sub-intervals containing a MMN in wakefulness did not significantly differ from the same intervals in sleep.

Low Frequency Separation Condition

The grand average and difference wave forms are shown in Figure 3.4 while Table 3.4 presents the mean amplitude of each sub-interval in the subtraction wave forms. A large and long duration negativity is clearly seen in the reading difference wave. It was significantly greater than zero at Fz in the 100 to 200 msec intervals, at Cz in the 100 and 150 msec intervals and at Pz in the 150 msec interval. The mean amplitudes in the 100 to 200 msec intervals were larger at Fz and Cz than at Pz. The wave forms in

this condition were computed on six subjects while those in all other conditions were computed on 13 subjects. It is possible that the large negativity in the low frequency condition might have been an artifact of the composition of the sample rather than a true reflection of the experimental manipulation. To evaluate this possibility, the reading data for the standard, high deviant probability and middle frequency separation conditions were again analysed but only with those six subjects used in the low frequency separation condition. Although the negativity was observed in these wave forms, it was generally found to be significantly different from zero only in the interval overlapping the maximum negativity. In the standard condition, this occurred in the 150 msec interval at Fz, Cz and Pz while in the high deviant probability condition, this occurred in the 50 msec interval at Fz and Cz. The negativity in the middle frequency separation condition was significant in the 50 msec interval at Cz.

Although relatively large negative amplitudes were recorded in the counting condition, no statistical differences were found in the 50 to 250 msec intervals except at Pz (200 msec interval). There were no statistical difference in the mean amplitude between electrode sites in these intervals.

During sleep, a large negativity was found which was similar to that found in the reading subtraction wave forms. During late stage 2, the negative amplitude was statistically different from baseline at Cz and Pz in the 100 and 150 msec intervals. In REM this occurred at Fz in the 150 msec interval. As in wakefulness, there

were no statistical differences in amplitude between electrodes although they tended to be larger at Cz than at Fz and Pz. The amplitude of the sub-intervals containing a MMN in wakefulness did not significantly differ from the same intervals within sleep.

Discussion

A set of criteria was established for defining the Mismatch Negativity (MMN). Accordingly, the deviant wave form was required to be significantly more negative than the standard in the 50 to 200 msec latency period. This would appear as a slow negativity in the difference wave obtained by subtracting the standard from the deviant wave form. The topography of this negativity was to be largest at frontal and central electrode sites and smallest at the parietal site.

Standard Condition

The broad negativity observed in the subtraction wave forms in the reading session resembled the negativity reported by Naatanen and his colleagues. The onset of this negativity began at about the peak latency of N1 and continued for 150 to 200 msec. The mean amplitude in the intervals overlapping its peak latency were found to be significantly different from zero. The amplitude and peak latency of the negative deflection were almost identical to that recorded by Naatanen et al. (1978, 1980a) in their original studies of the MMN. Its distribution appeared to be somewhat more central than that reported by Naatanen et al. (1982, 1983). There seems

therefore to be good evidence to suggest that this was a true MMN.

The difference wave in the counting session disclosed a small negativity occurring at about the same time as that found in the reading session. While this may reflect MMN-related activity, the amplitude of this negativity was smaller and its duration shorter in contrast to the reading session. In none of the intervals did the negative difference wave deviate significantly from the zero baseline. Moreover, the negativity that was centered around the peak latency of N1 did not merge with a later negative-positive ("N2b-P3") deflection as noted by Naatanen et al. (1983). For these reasons, it is doubtful that this small negativity represents a true MMN. Naatanen et al. however note that in easy detection tasks (for example, when deviants are clearly different from standards), the MMN may overlap with the N2 and thus not be distinguishable from it.

The primary reason, however, for showing the wave forms from the counting sessions was to provide physiological evidence of differences in processing between the reading and counting sessions. As was apparent, the later negative-positive complex (200-400 msec) in the counting subtraction wave forms coincided in time with the N2-P3 complex in the grand average wave forms to deviant stimuli. The N2-P3 complex is a measure of conscious, effortful processing (i.e. subjects were in fact counting the deviant stimuli) (Donchin et al., 1978; Pritchard, 1981). The absence of this complex would suggest that the processing related to conscious discrimination was not carried out. The negativity seen in the reading sessions could not be attributed to the N2-P3 complex since it was not elicited. Thus,

the negativity found in the reading difference wave could more likely be explained as MMN-related processes than the conscious and effortful processing reflected by N2b-P3.

There was very little evidence of the MMN in the standard condition during sleep. In early stage 2 and SWS, the deviant wave form was generally more positive than the standard wave form within the 50 to 200 msec interval. This was contrary to what would be expected of the MMN. During late stage 2 and REM sleep, a small negative deflection was found in the difference wave form in contrast to the broad negativity found in the reading session. The amplitude in the intervals overlapping this negativity were not statistically greater than zero. The morphology of the sleep negativity did not resemble that found in the reading session and cannot therefore be interpreted as evidence of the MMN in sleep.

Deviant Probability Condition

A negative shift was observed in the deviant relative to the standard wave forms in the high deviant probability condition. Its onset and offset coincided with the onset and offset of N1. This negativity thus began earlier than that in the standard condition. The scalp topography of this negativity was clearly fronto-central and its amplitude was smaller than that in the standard condition. This negativity was suggested to be the MMN. The reduction in amplitude relative to that in the standard condition is consistent with the study of Naatanen et al. (1983) who reported the amplitude of the MMN was inversely related to the probability of the deviant stimulus. They did not find the onset of this negativity varied as

a function of deviant probability.

During sleep, large differences between deviant and standard wave forms occurred soon after stimulus onset in both late stage 2 and REM sleep. The grand average difference wave forms showed the onset of this negativity began prior to stimulus onset in REM sleep. The grand average subtraction wave form was based on eight subjects, seven of whom showed a negativity beginning 10 to 60 msec after stimulus onset. In one subject, a large negativity began in the pre-stimulus interval and peaked at stimulus onset. The small pre-stimulus negativity in the grand average wave form was therefore due to this single subject. Despite the relatively large amplitude in the 50 msec interval in late stage 2, the difference between deviant and standard wave forms was not statistically different from zero. The negativity in the sleep difference wave forms therefore does not fit the criteria of the MMN. Although the negativity has a long duration and a fronto-central distribution, its onset began earlier than what would be expected of a MMN.

Frequency Separation Conditions

Sams et al. (1985b) reported the amplitude of the MMN decreased as the frequency separation between deviant and standard stimuli was reduced. While the frequency separations between deviant and standard stimuli in their study ranged from 2 to 32 Hz, the frequency separations in this study were 50, 250 and 1000 Hz. A comparison of the MMN in their widest frequency separation condition (32 Hz) with the negativity in the low frequency separation condition (50 Hz) in this study showed that the peak amplitudes were

approximately the same in latency and amplitude. However in this study, the peak amplitudes in the reading subtraction wave forms did not increase with wider frequency separations as might have been expected. Instead the negativity was attenuated in the standard and middle frequency separation conditions.

In the middle frequency separation condition the negativity began at the the same time as that in the wide frequency separation ("standard") condition and displayed a similar central distribution.

Its amplitude was less than that in the wide frequency separation condition. It was somewhat larger at frontal and central than parietal sites. In the counting session, a large negativity was found to overlap the N1 latency period. It had a clear fronto-central distribution and a peak latency which was slightly later than that of N1. This negativity was followed by N2b-P3 related activity. The data in the counting subtraction wave form resembled the results reported by Naatanen et al. (1983) which were suggested to show the MMN occurring at the same time period as the N2-P3 complex. The MMN appeared in their difference wave forms as a slow ramp-like negativity which merged at its peak with the well defined N2b-P3 related wave form. In the present study the earlier occurring negativity did not merge in any of the conditions with the second negativity but rather returned to baseline. This very early negativity is therefore probably not a MMN. It may represent either a sensory effect (the standard and deviant were of a different frequency) or a refractory effect (the deviant was presented much more infrequently than the standard). During late stage 2, there

was no sign of the MMN, the deviant wave form was more positive than the standard wave form for about 350 msec after stimulus onset. During REM sleep, negativity in the difference wave generally fit the criteria of the MMN. It occurred well within the established latency range. Furthermore its onset and amplitude were similar to that in the found in the reading session although its duration was somewhat shorter. However, this apparent MMN did not vary significantly from baseline.

The strongest evidence for the presence of the MMN within sleep came from the low frequency separation condition. In the reading condition, a significant fronto-central negativity was observed in the 100 to 200 msec intervals. The MMN in the reading session appeared to have also been recorded in late stage 2 and REM sleep. The peak latencies of the negative deflections in late stage 2 and REM occurred somewhat earlier than in the reading session which appeared to have a central distribution. During late stage 2, the mean amplitude in the interval overlapping the peak amplitude were significantly different from zero. The fact that this did not occur in REM sleep appeared to be due to a proportionately greater degree of subject variability. Since the negativities recorded in the subtraction wave forms in late stage 2 and REM sleep generally satisfy the criteria set forth in this study, they would accordingly be classified as the MMN.

Overview

The onset latency, duration and scalp topography of the negativity in reading wave forms were approximately the same across

the experimental manipulations. In general, the onset of this negativity began about 50 to 100 msec after stimulus onset while its offset occurred at about 250 to 300 msec. Moreover, the negativity tended to be largest in the frontal and central regions with the mean amplitudes in the interval overlapping the peak latency generally being statistically greater than zero. We did not record from temporal electrodes and thus were not able to show a mismatch effect over the regions corresponding to the primary and association areas of the auditory cortex (Hari et al., 1985; Sams et al., 1985a). Nevertheless, the negativity recorded in the reading sessions was similar to that reported by Naatanen et al. (1978, 1980a) and thus suggested to be the MMN. It did not appear as a well defined negative deflection in deviant wave forms (Sams et al., 1985b, 1986) but rather as a slight negative shift in deviant wave forms relative to standard wave forms (Naatanen et al., 1978, 1980a, 1983). This slight shift appears to have been recorded in another study conducted outside of the Finnish laboratory. The figures from the third study by Fitzgerald and Picton (1984) suggested the differences between deviant and standard wave forms appear as an increased negativity in the deviant wave forms. In this study, three different deviant stimuli were randomly presented within a train of standard stimuli. In all conditions, the 1000 Hz standard stimulus was presented at a probability of 80.5%. In the first condition, 1800, 1200 and 1050 Hz deviant stimuli were presented were presented at probabilities of 13.5%, 4.5% and 1.5% respectively. In the second condition, the probability of the 1800

and 1050 Hz deviants was reversed. Subjects were required to press a button every time they detected one of the deviant stimuli. The third and fourth conditions were identical to the first and second conditions except that subjects were required to read a book and ignore all auditory stimuli. Although Fitzgerald and Picton (1984) stated they found no evidence of the MMN, the deviant wave forms recorded while subjects were reading (Fig. 9) were slightly more negative than the standard wave forms during the N1-P2 latency period.

The differences between deviant and standard stimuli did not occur as consistently in sleep as in wakefulness. Indeed, if the criteria employed for the identification of the MMN are strictly followed, the MMN was elicited during sleep only in the low frequency condition. In the high deviant probability condition an apparent MMN was observed in both stage 2 and REM sleep, only that in REM reaching significance. The amplitude was somewhat larger and the onset latency earlier than in the reading session. In the standard condition, the duration of the negativity seen in the sleep subtraction wave forms was very short compared to the MMN in the reading session. In the middle frequency separation condition, the subtraction wave form fell below baseline in late stage 2 while in REM a significant negativity could not be identified. On the other hand, it is difficult to consider the negativity observed in the subtraction wave forms in sleep as being random activity. A well defined negativity was recorded during REM sleep in all but the standard condition. In late stage 2, a large negativity was

observed in the high deviant probability and low frequency separation conditions. The maximum amplitude of the negativity in REM sleep in fact appeared to decrease with increasing frequency separation as was found in the reading wave forms. In addition, the subtraction wave forms indicated the duration of the negativity in REM sleep was shorter in the standard and middle frequency separation conditions than in the low frequency separation condition. This suggests that the total duration of the MMN is a reflection of the time required to detect a mismatch. This issue has not been addressed in the literature for the hypothesized automatic MMN-related process. However, in the reading sessions, the duration of the negativity in the standard condition was visibly shorter than in the middle and low frequency separation condition. It would appear that the mismatch process is faster in sleep since the duration of the negativity was shorter in sleep than the reading session for all three conditions. The data recorded in sleep for the high deviant probability condition cannot be explained as easily. The expected effect of increasing stimulus probability would have been a reduction in amplitude (Naatanen et al., 1983). The opposite occurred as the amplitude in this condition was larger and more pronounced in sleep than in the standard condition. This apparent, early MMN was replicated in both REM and late stage 2 and is therefore not likely a random effect.

These data are therefore somewhat different from those reported by Sams et al. (1986). They found no evidence of the MMN in sleep. They limited their testing period to the early evening. As noted in

the standard condition in this thesis, this is the period in which subjects are least likely to display a MMN. Subjects may show a MMN in stage 2 in the second half of the night.

The first study of this thesis has shown that the N1 is largely attenuated in sleep whereas the amplitudes of P1 and P2 were found to be larger in sleep than wakefulness. The difference between wakefulness and sleep was attributed to the removal of a slow, attention-related, negative component labelled "wNd". Indeed the waking N1 was suggested to consist primarily of this slow component. The large decrease in the sleep N1 amplitude and large increase in the sleep N2 were found in both the deviant and standard wave forms. There was also a general tendency for P1 and P2 to be larger in sleep than wakefulness. The morphology of the sleep wave forms were therefore quite different from the waking wave forms. We do not know of any studies which have examined the effect of deviant and standard stimuli on the individual peak components in sleep. Although Sams et al. (1986) used a similar paradigm, they restricted their investigation, as did this study, to an analysis of the MMN. An examination of their figures however showed a similar decrease in N1 amplitude. If in fact the negativity recorded during sleep in this study corresponds to the MMN, then the decrease in N1 amplitude would provide further evidence that the MMN is elicited independently of attention-related processing.

Sams et al. (1986) suggested that the "generator mechanisms of the ERP [Event-Related Potential] components specific to stimulus deviance, are either related to conscious, active stimulus

discrimination, or that these mechanisms need a certain degree of general cortical activation in order to function, although they may be in awake stage, independent of attention." (p.393) If we accept this conclusion, then the MMN related activity is at least partially, if not entirely endogenous (i.e. it changes with the level of arousal). In the present study, only the large negativity recorded during late stage 2 in the low frequency separation condition appeared to fulfilled our rather strict criteria of the MMN component. However, the negativity in other conditions observed during sleep generally satisfied one or more of these criteria. As such, they showed a strong resemblance to the MMN recorded in wakefulness. The consistency with which the sleep negativity was found, although frequently not significant, suggested an effect of stimulus deviance had been recorded in sleep. Although not conclusive, the possible presence of a MMN in sleep supports the hypothesis that the MMN is an exogenous component.

Table 3.1

Mean Amplitudes (uV) and Standard Error (in parentheses)
of Subtraction Wave Forms in
Standard Condition

Stage	Time Interval (ms)								
	50	100	150	200	250	300	350	400	450
=====									
Read									
Fz	-0.26 (0.36)	-1.21* (0.56)	-1.21* (0.57)	-0.70* (0.36)	0.08 (0.37)	0.39 (0.51)	-0.43 (0.58)	-1.24+ (0.32)	-1.33+ (0.26)
Cz	-0.44 (0.30)	-1.19* (0.55)	-1.62+ (0.51)	-0.88* (0.34)	0.29 (0.41)	0.63 (0.61)	-0.09 (0.53)	-0.97+ (0.28)	-1.31+ (0.35)
Pz	-0.34 (0.30)	-0.67 (0.39)	-1.25+ (0.41)	-0.58* (0.22)	-0.07 (0.36)	0.76 (0.47)	0.51 (0.46)	-0.19 (0.34)	-0.72* (0.35)

Count									
Fz	-0.46 (0.32)	-0.55 (0.65)	-0.33 (0.73)	-2.84+ (0.76)	1.53 (1.02)	5.08+ (0.97)	1.96* (0.89)	-1.86* (0.93)	-3.82+ (0.73)
Cz	-0.46 (0.30)	-0.23 (0.57)	-1.36 (0.84)	-2.61+ (0.78)	5.11+ (1.13)	9.25+ (1.21)	5.57+ (1.06)	-0.13 (1.03)	-2.93+ (1.01)
Pz	-0.17 (0.24)	-0.09 (0.42)	-0.03 (0.69)	-0.31+ (0.51)	5.01+ (0.82)	9.11+ (0.99)	8.06* (1.06)	2.79 (1.09)	-0.32 (1.08)

Late 2									
Fz	-0.22 (0.51)	0.78 (0.71)	0.91 (0.86)	0.75 (0.93)	1.99* (1.00)	0.72 (1.01)	0.00 (1.06)	-1.20 (0.92)	-2.01 (1.16)
Cz	-0.05 (0.56)	0.16 (0.75)	1.07 (0.86)	1.18 (1.07)	0.90 (0.92)	-1.18 (0.93)	-1.42 (1.05)	-1.59 (1.29)	-1.45 (1.78)
Pz	0.42 (0.54)	0.62 (0.58)	1.45 (0.76)	1.32 (0.78)	0.08 (0.63)	-1.25 (0.93)	-1.17 (1.13)	-1.63 (1.00)	-1.04 (1.20)

REM									
Fz	0.07 (1.08)	-0.44 (1.27)	0.38 (1.39)	1.36 (1.17)	0.76 (1.15)	0.30 (1.31)	-0.01 (0.89)	-0.32 (0.99)	-0.01 (0.52)
Cz	0.05 (0.94)	-0.13 (1.13)	1.02 (1.40)	1.82 (1.22)	0.72 (1.54)	0.29 (1.66)	-0.02 (1.04)	0.45 (0.78)	0.22 (0.45)
Pz	-0.02 (0.54)	0.51 (0.66)	1.39 (0.83)	1.05 (0.90)	0.03 (1.10)	1.20 (1.03)	1.10 (0.78)	1.38* (0.54)	0.64 (0.75)

* p<.05

+ p<.01

Table 3.2

Mean Amplitudes (uV) and Standard Error (in parentheses)
of Subtraction Wave Forms in
High Deviant Probability Condition

Stage	Time Interval (ms)								
	50	100	150	200	250	300	350	400	450
=====									
Read									
Fz	-0.96+ (0.34)	-0.83* (0.39)	-0.49 (0.48)	-0.36 (0.40)	-0.30 (0.37)	-0.20 (0.40)	-0.39 (0.40)	-0.52 (0.39)	-0.80 (0.57)
Cz	-0.94+ (0.33)	-0.79* (0.38)	-0.49 (0.40)	-0.52* (0.27)	-0.10 (0.35)	-0.02 (0.31)	-0.33 (0.36)	-0.78* (0.38)	-0.73 (0.48)
Pz	-0.64 (0.37)	-0.52 (0.36)	-0.43 (0.36)	-0.60* (0.32)	-0.29 (0.45)	0.10 (0.33)	-0.09 (0.43)	-0.65 (0.44)	-0.28 (0.42)

Count									
Fz	-0.70* (0.30)	0.15 (0.38)	0.65+ (0.21)	-1.33* (0.61)	1.09 (0.73)	2.37+ (0.47)	0.92* (0.49)	-0.50 (0.85)	-1.70* (0.79)
Cz	-1.50+ (0.47)	-0.08 (0.37)	-0.38 (0.35)	-1.34* (0.59)	2.82+ (0.71)	5.07+ (0.63)	3.28+ (0.47)	0.01 (0.92)	-2.10* (0.90)
Pz	-1.01* (0.38)	-0.21 (0.35)	0.23 (0.32)	-0.30 (0.46)	2.59+ (0.64)	4.96+ (0.70)	5.09+ (0.60)	1.42* (0.71)	-0.75 (0.69)

Late 2									
Fz	-1.31 (1.26)	-0.87 (1.00)	0.44 (1.01)	1.33 (0.81)	2.50+ (0.72)	0.31 (0.86)	-0.56 (1.04)	-0.74 (1.72)	-3.57 (2.67)
Cz	-1.43 (1.45)	-1.32 (0.89)	0.05 (0.79)	0.65 (0.46)	0.33 (1.03)	-2.37 (2.09)	-3.05 (2.38)	-2.92 (2.75)	-4.05 (2.99)
Pz	-1.19 (1.27)	-1.16* (0.57)	-1.10* (0.47)	0.00 (0.66)	-1.08 (1.39)	-2.16 (2.09)	-2.31 (2.02)	-2.94 (1.97)	-2.91 (1.99)

REM									
Fz	-1.31+ (0.47)	-0.60 (0.81)	-0.08 (0.78)	0.34 (0.93)	0.36 (1.03)	0.30 (0.96)	-0.05 (1.15)	0.35 (1.04)	0.90 (1.33)
Cz	-1.04* (0.42)	-0.67 (0.48)	0.35 (0.75)	0.51 (1.25)	0.52 (1.61)	1.00 (1.53)	0.65 (1.47)	0.70 (1.35)	0.94 (1.53)
Pz	0.13 (0.31)	-0.83 (0.56)	-0.15 (0.37)	0.00 (0.55)	0.24 (0.80)	1.08 (0.97)	0.85 (0.66)	1.10 (0.60)	0.85 (0.65)

* p<.05

+ p<.01

Table 3.3

Mean Amplitudes (uV) and Standard Error (in parentheses)
of Subtraction Wave Forms in
Middle Frequency Separation Condition

Stage	Time Interval (ms)								
	50	100	150	200	250	300	350	400	450
=====									
Read									
Fz	-0.53 (0.38)	-0.70 (0.63)	-0.67 (0.65)	-0.68 (0.50)	-0.76* (0.42)	-0.36 (0.62)	-0.78 (0.58)	-1.05 (0.60)	-1.06* (0.51)
Cz	-0.65* (0.29)	-0.83 (0.54)	-0.75 (0.52)	-0.09 (0.31)	-0.27 (0.35)	-0.36 (0.49)	-0.55 (0.45)	-0.66 (0.58)	-0.85* (0.43)
Pz	-0.30 (0.25)	-0.56 (0.42)	-0.51 (0.49)	-0.09 (0.29)	-0.20 (0.32)	-0.02 (0.41)	0.10 (0.49)	0.32 (0.47)	0.06 (0.42)

Count									
Fz	-1.21* (0.68)	-1.74* (0.84)	-0.40 (0.87)	-2.46+ (0.87)	-1.03 (0.64)	2.18+ (0.63)	1.42* (0.62)	-0.17 (0.83)	-1.16 (1.55)
Cz	-0.78 (0.64)	-1.11 (0.83)	-0.59 (0.87)	-2.02* (0.91)	1.91* (0.77)	6.04+ (0.88)	5.09+ (0.98)	1.99* (0.91)	-1.49 (0.86)
Pz	-0.26 (0.39)	-0.75 (0.50)	-0.24 (0.51)	-0.40 (0.61)	2.48+ (0.72)	6.34+ (0.73)	6.98+ (0.93)	4.29+ (0.72)	1.15 (0.88)

Late 2									
Fz	2.16* (0.80)	2.84* (1.31)	1.57* (0.77)	1.55 (0.94)	1.13 (0.97)	0.45 (1.20)	-0.41 (1.22)	-1.48 (1.22)	-2.49 (1.82)
Cz	2.19* (1.06)	2.65 (1.44)	2.25 (1.60)	1.49 (0.98)	1.12 (1.06)	0.39 (1.34)	0.12 (1.33)	-0.39 (1.54)	-1.40 (1.85)
Pz	1.39 (0.79)	1.38 (1.02)	1.12 (1.27)	1.08 (0.74)	1.46 (0.86)	0.71 (1.05)	0.35 (1.31)	0.12 (1.36)	-0.59 (1.52)

REM									
Fz	0.13 (0.36)	-0.41 (0.52)	-0.27 (0.63)	-0.39 (0.52)	0.12 (0.51)	-0.42 (0.57)	-1.53* (0.78)	-0.69 (0.70)	-0.22 (0.36)
Cz	0.08 (0.51)	-0.59 (0.97)	-0.52 (0.97)	-0.03 (0.75)	0.42 (0.33)	-0.62 (0.72)	-1.44* (0.71)	-0.73 (0.68)	-0.69 (0.68)
Pz	0.11 (0.63)	-0.42 (0.99)	-0.06 (0.93)	0.21 (0.74)	0.21 (0.60)	-0.54 (0.58)	-0.60 (0.62)	-0.38 (0.67)	-0.86 (0.55)

* p<.05

+ p<.01

Table 3.4

Mean Amplitudes (uV) and Standard Error (in parentheses)
of Subtraction Wave Forms in
Low Frequency Separation Condition

Stage	Time Interval (ms)								
	50	100	150	200	250	300	350	400	450
Read									
Fz	-0.59 (0.44)	-1.19* (0.55)	-2.31+ (0.62)	-1.16* (0.48)	-0.48 (0.44)	-1.17* (0.48)	-1.64* (0.71)	-1.26 (0.79)	-1.59 (0.87)
Cz	-0.83 (0.41)	-1.53* (0.63)	-2.48+ (0.63)	-1.26 (0.66)	-0.49 (0.56)	-0.99* (0.45)	-1.56 (0.82)	-1.10 (0.90)	-1.37 (0.98)
Pz	-0.58 (0.52)	-0.98 (0.79)	-1.55* (0.72)	-0.90 (0.71)	-0.56 (0.63)	-0.71 (0.55)	-0.99 (0.73)	-0.64 (0.77)	-0.52 (0.77)
Count									
Fz	-0.30 (0.67)	-1.19 (0.89)	-0.16 (1.07)	-0.93 (1.13)	-0.73 (1.15)	2.56* (1.20)	3.77+ (0.73)	2.31 (1.53)	2.15 (1.28)
Cz	-0.35 (0.53)	-1.80 (1.08)	-0.08 (0.98)	-2.25 (1.26)	-0.04 (1.40)	5.99+ (0.96)	7.39+ (0.99)	5.24+ (1.55)	2.31 (1.74)
Pz	0.14 (0.67)	-1.34 (1.17)	-0.04 (0.80)	-1.05+ (0.53)	0.94 (1.08)	5.30+ (0.96)	7.71+ (1.15)	6.94+ (1.23)	4.29+ (1.08)
Late 2									
Fz	0.18 (1.84)	-1.44 (1.20)	-1.16 (1.59)	-0.13 (2.33)	-0.85 (1.84)	0.59 (1.88)	1.18 (1.10)	1.46 (1.28)	0.07 (2.24)
Cz	-0.45 (1.32)	-2.18* (1.06)	-2.20* (1.10)	-1.30 (1.75)	-1.70 (1.54)	-0.07 (1.66)	0.15 (1.55)	-0.45 (1.63)	-0.80 (2.11)
Pz	-0.28 (0.60)	-1.32* (0.60)	-1.31* (0.67)	-1.09 (0.73)	-1.23 (1.03)	-0.67 (1.43)	-0.98 (1.56)	-1.04 (1.59)	-0.67 (1.08)
REM									
Fz	-0.36 (0.68)	-1.08 (1.07)	-0.62* (0.28)	0.03 (0.55)	-0.03 (0.46)	-0.30 (0.35)	-0.19 (0.82)	1.60 (1.22)	1.51 (1.57)
Cz	-0.60 (1.16)	-1.17 (1.16)	-0.31 (0.37)	0.30 (0.25)	-0.12 (1.04)	-0.51 (1.24)	0.12 (1.06)	1.68 (2.08)	-2.10 (2.31)
Pz	0.44 (1.18)	-0.88 (0.71)	-0.65 (1.02)	-0.26 (1.00)	-0.43 (1.00)	-1.11 (1.39)	-0.32 (1.24)	0.67 (1.74)	1.75 (1.45)

* p<.05

+ p<.01

Figure Legend

Figure 3.1 Grand average wave forms (upper half of figure) following standard (thin lines) and deviant (thick lines) stimuli in the Standard condition. 80 dB SPL tone pips (1000 Hz standards, 2000 Hz deviants) were monaurally presented with a duration of 50 msec (5 msec rise-fall times) at a rate of 1/2 sec. The standard and deviant stimuli were randomly presented at probabilities of .80 and .20 respectively. Averages were computed in wakefulness (reading and counting sessions) and the different stages of sleep. The N1-P2 complex was elicited by standard and deviant stimuli in wakefulness regardless of whether subjects were reading or counting. The large N2-P3 complex was only elicited when subjects counted the number of deviant stimuli. The difference wave forms (lower half of figure) were obtained by subtracting the standard from the deviant wave form. The difference wave in the reading session disclosed a broad negativity beginning at about 100 msec and continuing for about 200 msec and is suggested to be the Mismatch Negativity (MMN). In the counting session, the large negative-positive complex seen in the subtraction wave forms between 200 and 400 msec coincided in time with the N2-P3 complex and may have masked the MMN. In early stage 2 and SWS, the subtraction wave form was generally below baseline in the 50 to 200 msec interval contrary to what would be expected of the MMN. The small, short duration negativity found in late stage 2 and REM did not significantly differ from zero baseline. There is thus little evidence of a MMN at any time within

sleep for this condition.

Figure 3.2 Grand average wave forms (upper half of figure) to standard (thin lines) and deviant (thick lines) stimuli in the High Deviant Probability condition. Stimulus parameters were similar to those in the Standard condition except that standard stimuli were presented with a probability of .60 and deviants with a probability of .40. In wakefulness, the negativity in the subtraction wave forms (lower half of figure) were smaller than those recorded in the standard condition but were nevertheless significantly above baseline. In late stage 2 and REM, the negativity occurred earlier and had a larger amplitude than that found in the reading session. However, due to large inter-subject variability, only the early REM negativity attained significance. There is thus some, albeit weak, evidence that the MMN exists in sleep in this condition.

Figure 3.3 Grand average wave forms (upper half of figure) to standard (thin lines) and deviant (thick lines) stimuli in the Middle Frequency Separation condition. Stimulus parameters were similar to those in the Standard condition except that the deviant stimuli were presented with a frequency of 1250 Hz. The subtraction wave forms are presented in the lower half of the figure. The small, long duration negativity elicited in the reading session appears to reflect MMN-related activity, although it was not statistically different than baseline. In the counting session, a similar negativity of larger magnitude preceded the well-defined

negative-positive deflections (200-400 msec). There was no evidence of the MMN in late stage 2 whereas the negativity in the subtraction wave form in REM sleep was similar to that found in the reading session, although it too failed to attain statistical significance. There is thus little evidence that the MMN exists in sleep in this condition.

Figure 3.4 Grand average wave forms (upper half of figure) to standard (thin lines) and deviant (thick lines) stimuli in the Low Frequency Separation condition. Wave forms are based on the average of 6 subjects in wakefulness and and 5 subjects in NREM and REM. Stimulus parameters were similar to those in the Standard condition except that the deviant stimuli were presented with a frequency of 1250 Hz. The subtraction wave forms are presented in the lower half of the figure. The large negativity found in the reading session was statistically significant as were those observed in late stage 2 and REM sleep. There is thus good evidence that the MMN exists in sleep in this condition.

Figure 3.1

Grand average and difference wave forms in the standard condition.

STANDARD CONDITION

(Standard=1000 Hz; $p=.80$)
(Deviant= 2000 Hz; $p=.20$)

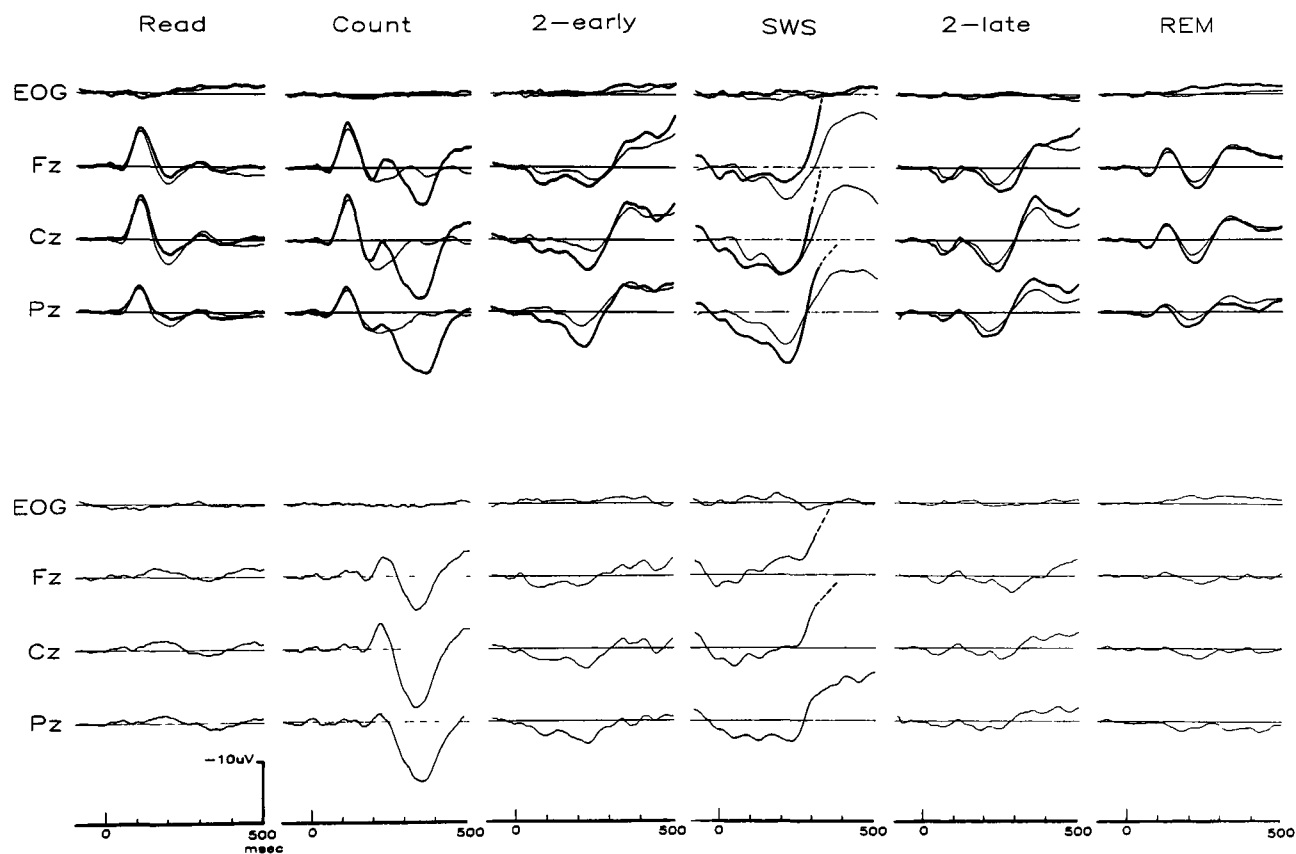


Figure 3.2

Grand average and difference wave forms in the
high deviant probability condition

HIGH DEVIANT PROBABILITY

(Standard=1000 Hz; $p=.60$)
(Deviant= 2000 Hz; $p=.40$)

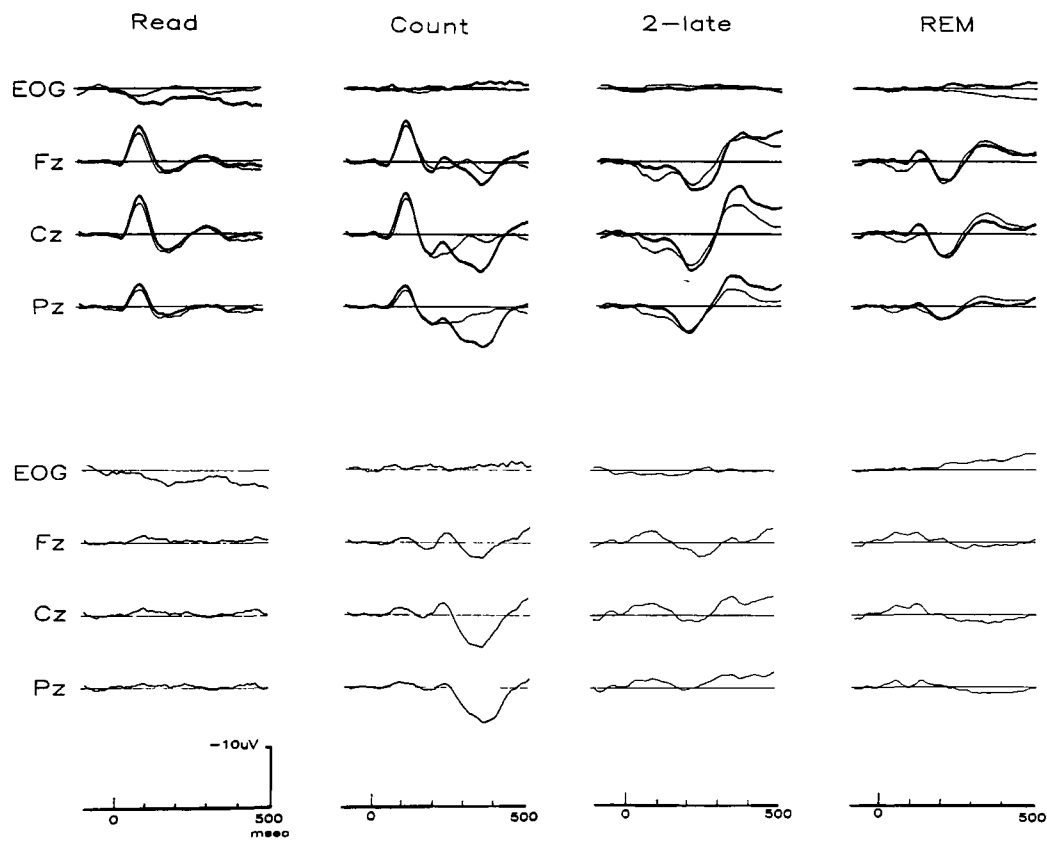
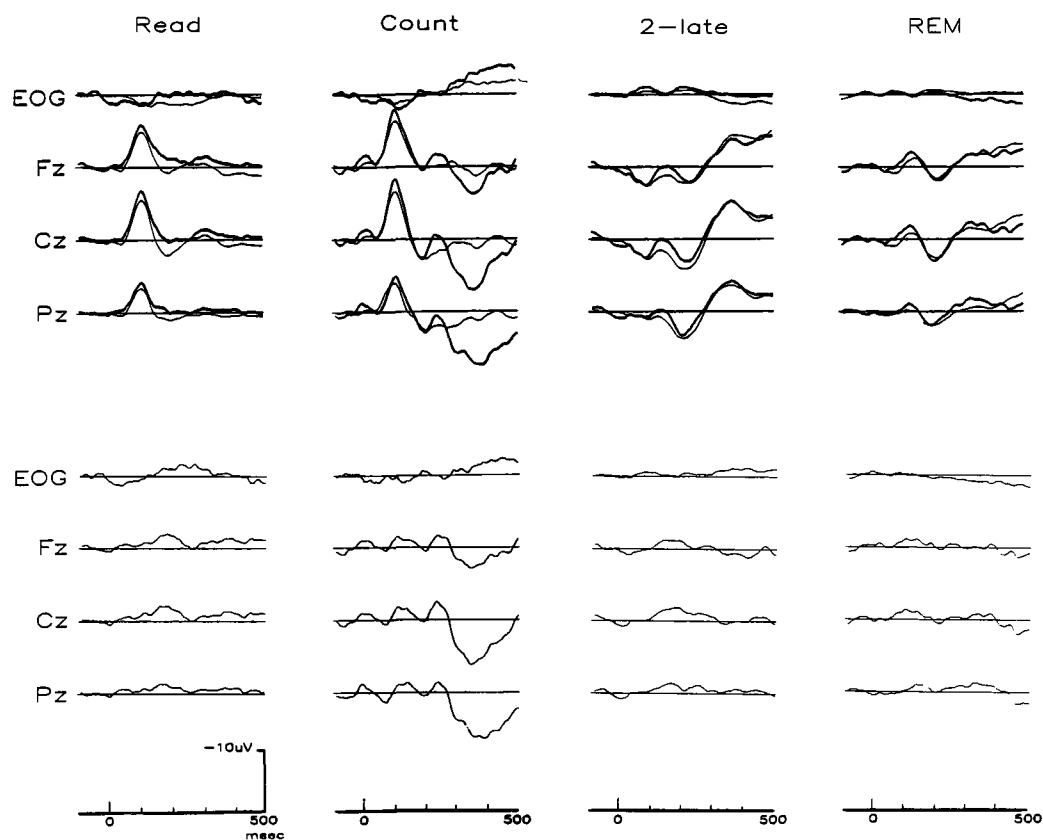


Figure 3.4

Grand average and difference wave forms in the
low frequency separation condition

LOW FREQUENCY SEPARATION

(Standard=1000 Hz; $p=.80$)
(Deviant= 1050 Hz; $p=.20$)



REFERENCES

- Alho, K., Sams, M., Paavilainen, P. and Naatanen, R. Small pitch separation and the selective-attention effect on the ERP. Psychophysiology, 1986, 23(2):189-197.
- Amadeo, M. and Shagass, C. Brief latency click evoked potentials during waking and sleep in man. Psychophysiology, 1973, 10(3):244-250.
- Anch, M. The auditory evoked brain response during adult human sleep. Waking and Sleeping, 1977, 1:189-194.
- Benson, D.F and Heinz, R.D. Single-unit activity in the auditory cortex of monkeys selectively attending left vs. right ear stimuli. Brain Research, 1978, 159:307-320.
- Bonnet, M.H., Johnson, L.C. and Webb, W.B. The reliability of arousal threshold during sleep. Psychophysiology, 1978, 15:412-416.
- Buchsbaum, M., Gillin, J. and Pfefferbaum A. Effect of sleep stage and stimulus intensity on auditory average evoked responses. Psychophysiology, 1975, 12(6):707-712.
- Campbell, K., Bell, I. and Deacon-Elliott, D. Stimulus-related influences on the K-Complex. In: W.P. Koella, E. Ruther and H. Schulz (Eds.), Neurophysiology of Sleep, Gustav Fischer Verlag, Stuttgart, 1985, 235-237.
- Campbell, K.B., Courchesne, E., Picton, T.W. and Squires, K.C. Evoked potential correlates of human information processing. Biological Psychology, 1979, 8:45-68.
- Campbell, K.B., McGarry, P.A. and Bell, I. Information processing during sleep: the effects of high stimulus intensity. In: W.P. Koella (Ed), Sleep '86, Gustav Fischer Verlag, Stuttgart, in press.

- Campbell, K.B. and Bartoli, E.A. Human auditory evoked potentials during natural sleep: the early components. Electroencephalography and Clinical Neurophysiology, 1986, 65:142-149.
- Csepe, V., Karmos, G. and Molnar, M. Evoked potential correlates of stimulus deviance during wakefulness and sleep in cat-animal model of Mismatch Negativity. Electroencephalography and Clinical Neurophysiology, in press.
- Davis, H. Principles of electric response audiometry. The Annals of Otology, Rhinology and Laryngology, supplement 28, 85(3), 1976.
- Davis, H. and Zerlin, S. Acoustic relations of human vertex potential. Journal of the Acoustical Society of America, 1966, 39:109.
- Davis, H., Mast, T., Yoshie, N. and Zerlin, S. The slow response of the human cortex to auditory stimuli recover process. Electroencephalography and Clinical Neurophysiology, 1966, 21:105-113.
- Davis, H., Osterhammel, P.A., Wier, C.C and Gjerdingen, D.B. Slow vertex potentials: Interactions among auditory, tactile, electric and visual stimuli. Electroencephalography and Clinical Neurophysiology, 1972, 33:537-545.
- Dawson, G.D. A summation technique for the detection of small evoked potentials. Electroencephalography and Clinical Neurophysiology, 1954, 6:65-84.
- Deacon-Elliott, D., Bell, I. and Campbell, K.B. Estimation of auditory thresholds during sleep using brainstem auditory evoked potentials (BAEP). (submitted).
- Desmedt, J.E., Brunko, E. and Debecker, J. Maturation and sleep correlates of the somatosensory evoked potential. In: J.E. Desmedt (Ed.), Clinical

Uses of Cerebral, Brainstem and Spinal Somatosensory Evoked Potentials:
Progress in Clinical Neurophysiology, 1980, 7:146-161.

- Desmedt, J.E., Debecker, J. and Robertson, D. Serial perceptual processing and the neural basis of changes in event-related potential components and slow potential shifts. In: J.E. Desmedt (Ed.), Cognitive Components in Cerebral Event-Related Potentials and Selective Attention: Progress in Clinical Neurophysiology, 1979, 6:53-79.
- Desmedt, J.E. and Robertson, D. Differential enhancement of early and late components of the cerebral somatosensory evoked potentials during forced-paced cognitive tasks in man. Journal of Physiology, 1977, 271:761-782.
- Donchin, E. Presidential Address, 1980: Surprise!...surprise?. Psychophysiology, 1981, 18:493-513.
- Donchin, E., Ritter, W. and McCallum, W.C. Cognitive Psychophysiology: The endogenous components of the ERP. In: E. Callaway, P. Tueting and S.H. Koslow (Eds) Event-Related Potentials In Man, Academic Press, New York, 1978, 349-441.
- Duncan-Johnson, C.C. and Donchin, E. The P300 component of the event-related potential as an index of information processing. Biological Psychology, 1982, 14:1-52.
- Eason, R., Harter, M. and White, C. Effects of attention and arousal on visually evoked cortical potentials and reaction time in man. Physiology and Behavior, 1969, 4:283-289.
- Erwin, R. and Buchwald, J.S. Midlatency auditory evoked responses: differential effects of sleep in the human. Electroencephalography and Clinical Neurophysiology, 1986, 65:383-392.
- Farley, G.R. and Starr, A. Middle and long latency auditory evoked potentials

- in cat. I: Component definition and dependence on behavioral factors. Hearing Research, 1983: 10:117-138.
- Fitzgerald, P.G. and Picton, T.W. Event-related potentials recorded during discrimination of improbable stimuli. Biological Psychology, 1983, 17:241-276.
- Fitzgerald P.G. and Picton, T.W. The effects of probability and discriminability on the evoked potentials to unpredictable signals. In: R. Karrer, J. Cohen and P. Tueting (Eds.), Brain and Information: Event-Related Potentials, New York Academy of Sciences, New York, 1984, 199-203.
- Ford, J.M, Roth, W.I. and Kopel, B.S. Auditory evoked potentials to unpredictable shifts in pitch, Psychophysiology, 1976, 13:33-39.
- Fruhstorfer, H. and Bergstrom, R.M. Human vigilance and auditory evoked responses. Electroencephalography and Clinical Neurophysiology, 1969, 27:346-355.
- Goff, G.D., Matsumiya, Y., Allison, T. and Goff, W.R. The scalp topography of human somatosensory and auditory evoked potential. Electroencephalography and Clinical Neurophysiology, 1977, 42:57-76.
- Hansen, H.C. and Hillyard, S.A. Endogenous brain potentials associated with selective auditory attention. Electroencephalography and Clinical Neurophysiology, 1980, 49:277-290.
- Hansen, H.C. and Hillyard, S.A. Selective Attention to Multidimensional Auditory Stimuli. Journal of Experimental Psychology: Human Perception and Performance, 1983, 9(1):1-19.
- Hansen, H.C. and Hillyard, S.A. Effect of stimulation rate and attribute cuing on event-related potentials during selective auditory attention.

Psychophysiology, 1984, 21(4):394-405.

Hari, R., Hamalainen, M., Ilmoniemi, R., Kaukoranta, E., Reininkainen, K.,

Salminen, J., Alho, K., Naatanen, R. and Sams, M. Responses of the primary auditory cortex to pitch changes in a sequence of tone pips: neuromagnetic recordings in man. Neuroscience Letters, 1984, 50:127-132.

Harter, M.R., Aine, C. and Schroeder, C. Hemispheric differences in the neural processing of stimulus location and type: Effects of selective attention on visual evoked potentials. Neuropsychologia, 1982, 20:421-438.

Hillyard, S.A. and Kutas, M. Electrophysiology of Cognitive Processes Annual Review of Psychology, 1983, 34:33-61.

Hillyard, S.A. and Picton, T.W. Event-related brain potentials and selective information processing in man. in Cognitive components in Cerebral Event-Related Potentials and Selective Attention (Ed) Desmedt, J.E. Progress in Clinical Neurophysiology, 1979, 6:1-52.

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

Hillyard, S.A., Munte, T.F. and Neville, H.J. Visual-spatial attention, orienting and brain physiology. In: M.I. Posner and O.S. Marin (Eds.), Mechanisms of attention: Attention and Performance, Erlbaum, Hillsdale, N.J., 1985, 63-84.

Hillyard, S.A. and Munte, T.F. Selective attention to color and location: An analysis with event-related brain potentials. Perception and Psychophysics, 1984, 36(2):185-198.

Jerger, J.J., Weibers, N.J., Sharbrough, F.W. and Jerger, S. Bilateral lesions of the temporal lobes. A case study. Acta-Oto-Laryngologica (Stockholm), 1969, 258:1-51.

Karlin, L. Cognition, preparation, and sensory-evoked potentials.

Psychological Bulletin, 1970, 73(2):122-136.

Kevanishvili, A.Sh. and Von Specht, H. Human low auditory evoked potentials during natural and drug-induced sleep. Electroencephalography and Clinical Neurophysiology, 1979, 47:280-288.

Kirk, R.E. Experimental design: Procedures for the behavioral sciences. (2nd edition), Monterey, California, Brooks/Coles, 1982.

Knight, R.T., Hillyard, S.A., Woods, D.L. and Neville, H. The effects of frontal and temporal-parietal lesions on the auditory evoked potential in man. Electroencephalography and Clinical Neurophysiology, 1980, 50:112-124.

Kok, A. van de Vijver, F.R. and Rooijakkers, J.A.J Effects of visual field, stimulus degradation, and level of practice on event-related potentials of the brain. Psychophysiology, 1985, 22(6):707-717.

Kooi, K.A., Topton, A.C. and Marshall, R.E. Polarities and field configurations of the vertex components of the human auditory evoked response: a reinterpretation. Electroencephalography and Clinical Neurophysiology, 1971, 31:116-169.

Kutas, M. and Hillyard, S.A. Event-related potentials to semantically inappropriate and surprisingly large words. Biological Psychology, 1980, 11:99-116.

Maskare, M., Campbell, K.B., Stelmack, R. and Knott, V. General purpose on-line signal averaging system for the Cromemco Z80 microcomputer. Psychophysiology, 22:244.

Mendel, M.I. Influence of stimulus level and sleep stage on the early components of the averaged electroencephalographic response to clicks

during all night sleep. Journal of speech and Hearing Research, 1975
17:5-17.

Mendel, M.I. and Goldstein, R. Stability of the early components of the averaged electroencephalographic response. Journal of speech and Hearing Research, 1969, 12:351-361.

Mendel, M.I. and Goldstein, R. Effect of sleep on the early components of the averaged electroencephalographic response. Arch. Klin. Exp. Ohr-U. Kehlk. Heilk, 1971a, 198:110-115.

Mendel, M.I. and Goldstein, R. Early components of the average electroencephalographic response to constant level clicks during all night sleep. Journal of speech and Hearing Research, 1971b, 14:819-828.

Mendel, M.I. and Kupperman, G.L. Early components of the averaged electroencephalographic response to constant level clicks during rapid eye movement. Audiology, 1974, 13:23-32.

McCarthy, G. and Wood, C.C. Scalp distributions of event-related potentials: an ambiguity associated with analysis of variance models. Electroencephalography and Clinical Neurophysiology, 1985, 62:203-208.

McCallum, W.C. and Curry, S.H. The form and distribution of auditory evoked potentials and CNVs when stimuli and responses are lateralized. In Motivation, Motor and Sensory Processes of the Brain: Electrical Potentials, Behaviour and Clinical Use, Progress in Brain Research (Vol. 54). H.H. Kornhuber and L. Deeck (Eds.). Amsterdam: Elsevier, 1980, pp.767-775.

McCallum, W.E., Curry, S.H., Cooper, R. Pocock, P.V. and Papakostopolous. Brain event-related potentials as indicators of early selective process in auditory target localization. Psychophysiology, 1983, 20:1-17.

- Michel, F., Peronnet, F. and Schott, G. A case of cortical deafness: clinical and electrophysiological data. Brain Language, 1980, 10:367-377.
- Naatanen, R. Selective attention and evoked potentials in humans - a critical review. Biological Psychology, 1975, 2:237-307.
- Naatanen, R. Processing Negativity: an evoked-potential reflection of selective attention. Psychological Bulletin, 1982, 92(3), 605-640.
- Naatanen, R. N2 and automatic versus controlled processes: A classification of N2 kinds of ERP components. Electroencephalography and Clinical Neurophysiology, (in press).
- Naatanen, R. Selective attention and stimulus processing: reflections in event-related potentials, magnetoencephalogram, and regional cerebral blood flow. In M.I. Posner and O.S. Marin (Eds.) Attention and Performance XI, 1985
- Naatanen, R. and Gaillard, A.W.K. The orienting reflex and the N2 deflection of the event-related potential (ERP). In Tutorials In Event Related Potential Research: Endogenous Components. A.W.K. Gaillard and W. Ritter (Eds.). North-Holland Publishing Company, 1983, 119-141.
- Naatanen, R., Gaillard, A.W.K and Mantysalo, S. Early selective-attention effect on evoked potential reinterpreted. Acta Psychologica, 1978, 42, 313-329.
- Naatanen, R., Gaillard, A.W.K. and Mantysalo, S. Brain potential correlates of voluntary and involuntary attention. In Motivation, Motor and Sensory Processes of the Brain: Electrical Potentials, Behaviour and Clinical Use, Progress in Brain Research (Vol. 54). H.H. Kornhuber and L. Deeck (Eds.). Amsterdam: Elsevier, 1980a, 54:343-348.
- Naatanen, R., Gaillard, A.W.K. and Varey, C.A. Attention effects on auditory

- EPs as a function of inter-stimulus interval. Biological Psychology, 1981, 13:173-187.
- Naatanen, R., Hukkanen, S. and Jarvilehto, T. Magnitude of stimulus deviance and brain potentials. In Motivation, Motor and Sensory Processes of the Brain: Electrical Potentials, Behaviour and Clinical Use, Progress in Brain Research (Vol. 54). H.H. Kornhuber and L. Deeck (Eds.). Amsterdam: Elsevier, 1980b, 54:337-342.
- Naatanen, R. and Michie, P.T. Early selective-attention effects on the evoked potential. A critical review and reinterpretation. Biological Psychology, 1979, 8:81-136.
- Naatanen, R., Sams, M., Jarvilehto, T. and Soininen, K. Probability of deviant stimulus and event-related brain potentials. In R. Sinz and M.R. Rosenzweig (Eds.) Psychophysiology, Elsevier, Amsterdam, 1983, 397-405.
- Naatanen, R., Simpson, M. and Loveless, N.E. Stimulus deviance and evoked potentials. Biological Psychology, 1982, 14:53-98.
- Nelson, D.A. and Lassman, F.M. Effects of intersignal interval on the human auditory evoked response. The Journal of the Acoustical Society of America, 1968, 1529-1532.
- Noldy-Cullum, N., McGarry, P.A. and Campbell, K.B. Late auditory evoked potentials as indicators of sleep onset. In: W.P. Koella (Ed), Sleep '86, Gustav Fischer Verlag, Stuttgart, 1986, in press.
- Okita, T. Slow negative shifts of the human event-related potential associated with selective information processing. Biological Psychology, 1981, 63-75.
- Ornitz, E.M., Ritvo, E.R., Carr, M.C., La Franchi, S. and Walter, R.D. The

effect of sleep onset on the auditory averaged evoked response.

Electroencephalography and Clinical Neurophysiology, 1967a, 23:335-341.

Ornitz, E.M., Ritvo, E.R., Everett, C.M., Panman, L.M. and Walter, R.

The variability of the auditory averaged evoked response during sleep and dreaming in children and adults. Electroencephalography and Clinical Neurophysiology, 1967b, 22:514-524.

Osterhammel, P.A., Davis, H., Wier, C.C. and Hirsh, S.K. Adult auditory evoked potentials in sleep. Audiology, 1973, 12:116-128.

Osterhammel, P.A., Shallop, J.K and Terkildsen, K. The effect of sleep on the auditory brainstem response (ABR) and the middle latency response (MLR). Scandinavian Journal of Audiology, 1985, 14:47-50.

Oswald, I., Taylor, A.M and Treisman, M. Discriminative responses to stimulation during human sleep. Brain, 1960, 83:440-453.

Parving, A., Salomon, G., Elberling, C., Larsen, B. and Lassen, N.A.

Middle components of the auditory evoked response in bilateral temporal lobe lesions. Scandinavian Journal of Audiology, 1980, 9:161-167.

Parasuraman, R. Auditory evoked potentials and divided attention.

Psychophysiology, 1978, 460-465.

Parasuraman, R. Effects of information processing demands on slow negative shift latencies and N100 amplitude in selective and divided attention.

Biological Psychology, 1980, 217-233.

Perrault, N. and Picton, T.W. Event-related potentials recorded from the

scalp and nasopharynx. I: N1 and P2. Electroencephalography and Clinical Neurophysiology, 1984a, 59:177-194.

Perrault, N. and Picton, T.W. Event-related potentials recorded from the

scalp and nasopharynx. I. N3, P3 and slow wave. Electroencephalography

- and Clinical Neurophysiology, 1984b, 59:261-278.
- Peronnet, F., Giard, M.H, Bertrand, O. and Pernier, J. The temporal component of the auditory evoked potential: A reinterpretation. Electroencephalography and Clinical Neurophysiology, 1984, 59:67-71.
- Peronnet, F and Michel, F. The asymmetry of the auditory evoked potential in normal man and in patients with brain lesions. Progress in Clinical Neurophysiology; vol.2, J.E. Desmedt (Ed.), Karger, Basel, 1977, 130-141.
- Picton, T.W., Goodman, W.S. and Bryce, D.P. Amplitude of evoked responses to tones of high intensity. Acta Otolaryngologica (Stockholm), 1970, 77-82.
- Picton, T.W., Hillyard, S.A., Krausz, H.I. and Galambos, R. Human auditory evoked potentials. I:Evaluation of components. Electroencephalography and Clinical Neurophysiology, 1974, 36:179-190.
- Picton, T.W. and Stuss, D.T. The component structure of the human event-related potentials. In Motivation, Motor and Sensory Processes of the Brain: Electrical Potentials, Behaviour and Clinical Use, Progress in Brain Research (Vol. 54). H.H. Kornhuber and L. Deeck (Eds.). Amsterdam: Elsevier, 1980, pp.17-19.
- Picton, T.W., Woods, D.L., Baribeau-Braun, J. and Healey, T.G. Evoked Potential Audiometry
- Price, L.J. and Kremen, I. Variations in behavioural response threshold within the REM period of human sleep. Psychophysiology, 1980, 17:133-140.
- Pritchard, W.S. Psychophysiology of P300. Psychological Bulletin, 1981, 89:506-540.
- Putnam, L.E. and Roth, W.T. Automatic elicitation of cognitive components by startling stimuli. In: J.W. Rohrbaugh, R. Johnson Jr. and R. Parasuraman

(Eds.), Eighth International Conference On Event-Related Potentials of the Brain (EPIC VIII), 1986, 391-393.

Rechtschaffen, A. and Kales, A. A Manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. BIS/BRI, UCLA, Los Angeles, CA, 1968.

Ritter, W., Simson, R., Vaughan, H.G. and Friedman, D. A brain event related to making of a sensory discrimination. Science, 1979, 203:1358-1361.

Roth, W.T., Blowers, G.H., Doyle, c.M. and Kopel, B.S. Auditory stimulus intensity effects of the late positive complex. Electroencephalography and Clinical Neurophysiology, 1982, 54:132-146.

Roth, W.T., Dorata, K.H. and Kopel, B.S. Intensity and task effects on evoked physiological responses to noise bursts. Psychophysiology, 1984 21:466-481.

Sams, M., Alho, K. and Naatanen, R. Short-term habituation and dishabituation of the Mismatch Negativity of the ERP. Psychophysiology, 1984, 21(4):434-441.

Sams, M., Hamalainen, M., Antervo, A., Kaukoranta, E., Reinikainen, K. and Hari, R. Cerebral neuromagnetic responses evoked by short auditory stimuli. Electroencephalography and Clinical Neurophysiology, 1985a, 61:254-266.

Sams, M., Paavilainen, P., Alho, K. and Naatanen, R. Auditory frequency and event-related potentials. Electroencephalography and Clinical Neurophysiology, 1985b, 62:437-448.

Sams, M., Paavilainen, P., Cammann, R., Alho, K., Reinikainen, K., and Naatanen, R. Event-related potentials to a pitch change in a repetitive auditory stimulus sequence during sleep. In: J.W. Rohrbaugh, R. Johnson

- Jr. and R. Parasuraman (Eds.), Eighth International Conference On Event-Related Potentials of the Brain (EPIC VIII), 1986, 391-393.
- Scherg, M. and Von Cramon, D. Two bilateral sources of the late AEP as identified by a spatio-temporal dipole model. Electroencephalography and Clinical Neurophysiology, 1985, 62:32-44.
- Scherg, M. and Von Cramon, D. Evoked dipole source potentials of the human auditory cortex. Electroencephalography and Clinical Neurophysiology, 1986, 65:344-360.
- Schwent, V.L., Hillyard, S.A. and Galambos, R. Selective attention and the auditory vertex potential. I. Effects of stimulus delivery rate. Electroencephalography and Clinical Neurophysiology, 1976a, 40:604-614.
- Schwent, V.L., Hillyard, S.A. and Galambos, R. Selective attention and the auditory vertex potential. II. Effects of signal intensity and masking noise, Electroencephalography and Clinical Neurophysiology, 1976b, 40:615-622.
- Schwent, V.L., Snyder, E. and Hillyard, S.A. Auditory evoked potentials during multichannel selective listening: Role of pitch and localization cues. Journal of Experimental Psychology: Human Perception and Performance, 1976c, 2, 313-325.
- Schneider, W., Dumasi, S.T and Shiffrin,, R.M. Automatic and control processing and attention. In: R. Parasuraman and D.R. Davies (Eds.), Varieties of Attention. Academic Press, Orlando, FL, 1984, 1-27.
- Shiffrin, R.M. and Schneider, W. Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. Psychological Review, 1977, 84:127-190.
- Simson, R., Vaughan, H.G.Jr. and Ritter, W. The scalp topography of

potentials associated with missing visual or auditory stimuli.

Electroencephalography and Clinical Neurophysiology, 1976, 40:33-42.

Simson, R., Vaughan, H.G.Jr. and Ritter, W. The scalp topography of potentials in auditory and visual discrimination tasks.

Electroencephalography and Clinical Neurophysiology, 1977, 42:528-535.

Snyder, E. and Hillyard, S.A. Long-latency evoked potentials to irrelevant, deviant stimuli. Behavioral Biology, 1976, 16:319-331.

Squires, K.C., Donchin, E., Herning, R.I and McCarthy, G. On the influence of task relevance and stimulus probability on event-related potential components. Electroencephalography and Clinical Neurophysiology, 1977, 42:1-14.

Steriade, M., Oakson, G. and Ropert, N. Firing rates and patterns of midbrain reticular neurons during steady and transitional states of the sleep-waking cycle. Experimental Brain Research, 1982, 46:37-51.

Stepheson, S.A. and Gibb, F.A. A balanced non-cephalic reference electrode. Electroencephalography and Clinical Neurophysiology, 1951, 3:237-240.

Streletz, L.J., Katz, L., Hohenberger, M. and Cracco, R.Q. Scalp recorded auditory evoked potentials and sonomotor responses: An evaluation of components and recording techniques. Electroencephalography and Clinical Neurophysiology, 1977, 43:192-206.

Stuss, D.T., Picton, T.W. and Cerri, A.M. Searching for the names of pictures: An event-related potential study. Psychophysiology, 1986, 23(2):215-223.

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

Ujjaszsi, J. and Halasz, P. Late component variants of single auditory evoked

- responses during NREM sleep stage 2 in man. Electroencephalography and Clinical Neurophysiology, 1986, 64:260-268.
- Vaughan, G.H.Jr. and Ritter, W. The sources of auditory evoked responses recorded from the human scalp. Electroencephalography and Clinical Neurophysiology, 1970, 28:360-367.
- Weitzman, E.D. and Kremen, H. Auditory evoked responses during different stages of sleep in man. Electroencephalography and Clinical Neurophysiology, 1964, 18:65-70.
- Williams, H.L., Morlock, H.C., Morlock, J.V. and Lubin, A. Auditory evoked responses and the EEG stages of sleep. Annals New York Academy of Sciences, 1964b, 112:172-181.
- Williams, H.L., Tepas, D.T. and Morlock, H.C. Evoked responses to clicks and electroencephalographic stages of sleep in man. Science, 1962, 138:685-686.
- Winer, B.J. Statistical principles in experimental design: 2nd Edition McGraw-Hill, New York, 1971.
- Woldorf, M., Hansen, J.C. and Hillyard, S.A. Selective attention alters human auditory sensory processing at 20-50 msec. In: J.W. Rohrbaugh, R. Johnson Jr. and R. Parasuraman (Eds.), Eighth International Conference On Event-Related Potentials of the Brain (EPIC VIII), 1986, 418-420.
- Wolpaw, J.R. and Penry, J.K. A temporal component of the auditory evoked response. Electroencephalography and Clinical Neurophysiology, 1975, 39:609-620
- Wolpaw, J.R. and Wood, C.C. Scalp distribution of human auditory evoked potentials. I. Evaluation of reference sites. Electroencephalography and Clinical Neurophysiology, 1982, 54:15-24.

- Woods, D.L. and Clayworth, C.C. Scalp topographies dissociate N1 and Nd components during auditory attention. In: J.W. Rohrbaugh, R. Johnson Jr. and R. Parasuraman (Eds.), Eighth International Conference On Event-Related Potentials of the Brain (EPIC VIII), 1986, 421-423.
- Woods, C.C., McCarthy, G., Squires, N.K., Vaughan, H.G., Woods, D.L. and McCallum, W.C. Anatomical and physiological substrates of event-related potentials: two case-studies. In: R. Karrer, J. Cohen and P. Tueting (Eds.), Brain and Information: Event-Related Potentials, New York Academy of Sciences, New York, 1984, 681-721.
- Wood, C.C. and Wolpaw, J.R. Scalp distribution of human auditory evoked potentials. II. Evidence for overlapping sources and involvement of auditory cortex. Electroencephalography and Clinical Neurophysiology, 1982, 54:25-38.

Note

1. Personal Communication with R. Naatanen at the Third International Evoked Potentials Symposium held in West Berlin, September 28th - October 1, 1986.

Appendix A

A Peak Detector Program for Event-Related Potentials

A PEAK DETECTOR PROGRAM FOR EVENT-RELATED POTENTIALS

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SUMMARY

A computer program, developed for peak detection of averaged evoked potential waveforms, is described. The program is able to automatically score up to 200 data files in a single session. The user is asked to define intervals (windows) in which a maximum peak is to be detected. The program can optionally search each EEG channel or a single "reference" channel from which all other channels will be compared. The mean amplitude of several data points can also be computed within a particular window. When evoked potentials are particularly noisy, it is possible to estimate the "signal" in the higher frequency background "noise". Because the program is written in BASIC, it can be readily transferred to many different computer systems.

A Peak Detector Program for Event-Related Potentials

The majority of laboratories define "components" of the averaged evoked potential (EP) according to a maximum peak deflection appearing within arbitrarily defined intervals. Thus, for example, a component such as "N1" might be defined as the maximum negative peak in the 70-150 ms post-stimulus interval while "P2" might be defined as the maximum positive peak in the 150-250 ms interval. The EP component is measured in terms of its maximum amplitude (usually relative to a baseline) and its latency at that amplitude. The popularity of this technique has been documented by Fabiani, Gratton, Karis and Donchin (in press). They examined the variability of measuring techniques for a late positive component, "P300". Of the 34 articles surveyed in the journal Psychophysiology from 1980 to 1984, almost half (15) used base-to-peak measurement exclusively. An additional five laboratories combined base-to-peak measurement with other techniques. Peak detection is but one of several ways of identifying components of the evoked potential. Admittedly, there are certain limitations to this method (Coles, Gratton, Kramer and Miller, in press; Donchin and Heffley, 1979; Picton and Stuss, 1980). Nevertheless, as Coles et al. point out, "the principal advantages of this measurement are its intuitive appeal and computational simplicity". It is easily standardized across laboratories and will therefore continue to be a common method of scoring EP waveforms.

Many evoked potential researchers still rely on manual scoring methods of "eye-balling" EP waveforms. Others employ a graphics terminal or oscilloscope display to establish co-ordinates typically through the use of a cursor. This simple task can become quite time-consuming given the large number of waveforms that must frequently be scored. The process of identifying peaks can, however, be easily performed by a computer and does not require sophisticated programming skills. A relatively simple peak detector program is therefore presented which can be easily adapted for use by a number of computer systems.

The following program was written to score data recorded using the EP system developed by Makasare et al. (1985). Programs for data acquisition, averaging and later off-line plotting were written in Z80 assembler. This system allows the presentation of up to 4 different stimuli and the on-line averaging of up to 8 analogue channels (i.e.: 4 x 8 or 32 separate averages). An A/D sweep consists of 300 samples per channel beginning 50 data points prior to stimulus onset. The scoring program itself was written in BASIC and is therefore readily transferrable to other CPUs. It consists of 2 routines. The first routine prompts the user for necessary information and then calls the second routine which performs the analysis. In many neurophysiology laboratories, negative peaks are recorded as an upward deflection and positive peaks as a downward deflection. This convention is used in the present program but can be easily changed, depending on the individual laboratory preference. The actual data, in accordance

with electronic convention, are stored as positive 'up' and negative 'down'. The valence of a peak is therefore changed during program output.

The time required to process a data file may range from less than one minute to several minutes depending upon the number of stimuli and channels to be scored, the number of defined windows (see section on Scoring Methods) and the type of analysis selected for each window. Since the same scoring criteria are often applied to two or more data files, the program was written to automatically analyze up to 200 consecutive files independent of user intervention. The computer system may therefore be tied up for several minutes if not hours depending on the number of files to be analyzed.

Scoring Methods:

A data file can contain a maximum of 8 digitized channels sorted for up to 4 different stimuli (i.e.: 32 different averages). At the beginning of the program, the user selects which stimulus set(s) and channel number(s) are to be scored. Stimulus sets are scored independently of each other. That is, the channel-averages recorded to a first stimulus are scored independently of channel-averages recorded to a second, third or fourth stimulus. The same channels are scored in each stimulus set.

A total of 10 windows can be defined to analyze the channel-averages within each stimulus set. A window refers to a time interval within recorded sweep times during which the analysis is to be conducted. If the start of a window begins at a latency

greater than the total sweep time, an error message is printed. The end of a window defaults to the total sweep time when the former value is greater than the latter value. Windows may overlap and therefore need not be mutually exclusive.

Each window may be scored by one of three methods. The first method, labelled "Reference Channel Analysis" (RCA), identifies a maximum peak within the window of a user-selected channel. Amplitude measures for other channels within that stimulus set are then made at (i.e.: referenced to) this peak latency. The second method, labelled "Separate Channel Analysis" (SCA), identifies a maximum peak within the window for each separate channel. Thus the latency measures across channels need not be identical. If a peak does not appear within a window for either RCA or SCA scoring methods, the message 'No Peaks' is printed. The third method, labelled "Data Point Averaging" (DPA), does not identify peaks. Rather, the mean amplitude of data points within a window is computed. The data points used to compute the mean amplitude can be printed by request. DPA is particularly applicable for the analysis of slow waves while RCA and SCA are more applicable for peak deflection analysis.

Scoring Options:

Two scoring options are applicable to the first and second scoring methods and a third option to all methods. Once a maximum peak has been identified, the first option labelled "Peak Percentage", can be used when high frequency activity (noise) is superimposed on a lower frequency waveform (the signal). For

example, in Figure 1, at approximately 550 ms, a large negative waveform (the signal) is visible. Superimposed on it are a number of smaller amplitude deflections (the noise). Since the scoring routine identifies the maximum negative peak in terms of the largest negative voltage within a user-defined window, the latency at which the largest voltage is detected may not necessarily be a good approximation of the large underlying negative deflection. To accomodate this problem and yet maintain the programs simplicity, an estimate of the signal is computed. A maximum peak is first defined through the RCA or SCA algorithm. The program then searches to the left and right of this peak latency until a user-defined percentage of the maximum peak amplitude is exceeded. The mean amplitude of all data points within this new sub-interval is used as an estimate of the true signal's amplitude. The mid-point of the sub-interval serves as the signal's estimated latency. As an example, the programs default value of 10% requests that an interval be defined containing all adjacent data points whose amplitude fall within 10% of the maximum negative voltage. If the user-defined value is zero (0), the program searches for a maximum peak within the window, exactly as it would normally in the RCA or SCA routine.

The algorithm for the "Peak Percentage option" involves several different steps. Starting at the apex of the maximum peak, the program compares its amplitude with those of data points to the left of the apex (i.e.: at earlier latencies). This comparison continues until the difference in amplitude exceeds

the user-specified percentage of the apex amplitude. The last data point fitting this criterion defines the start of an interval that will enclose the peak. The same process is followed for data points falling to the right of the apex (i.e.: at later latencies) thus defining an end to the interval. The mean amplitude of data points falling within this interval is then computed and printed. The mid-point of this interval defines the latency of the signal. In general, the difference between the mean amplitude and the amplitude of the maximum peak will tend to increase as the user-defined value increases (thereby defining a wider interval). This effect will be more pronounced for larger than smaller amplitude deflections. The difference in latency will increase as the peak deflection becomes more asymmetric or skewed.

The second scoring option, labelled "Valence of Peak(s)", is used to specify whether whether both negative and positive peaks should be identified within the defined-window or simply a particular valence (either positive- or negative-going peaks).

The third option, labelled "Point Interval", can be used when the inter-point interval (i.e., the A/D sampling rate) is not identical across all data files. Fast, high frequency EP components should be recorded with short inter-point intervals to provide adequate digital resolution. On the other hand, the later, lower frequency EP components are usually recorded with longer inter-point intervals. Since the scoring information entered for one set of data files may not necessarily be applicable to another

set of data files, the "Point Interval" option allows the user to define windows that will selectively analyze data files recorded at a specific sampling rate. For example, let us assume a particular set of files had an inter-point interval of 2 ms while another set of files had a point interval of 6 ms. Furthermore, assume 6 windows will be defined. The first 2 windows could be used to score those data files having a 2 ms point interval and the next 2 windows could score those files having a 6 ms point interval. As explained at the end of this section, the last 2 windows could be used to score both sets of data files. This requires that the user know the inter-point interval that was used to collect the data for a particular file. The Makasare et al. data files contain a good deal of file information, including the inter-point interval. Therefore, if the user does not (or cannot) specify the inter-point interval, the program will read it automatically. For each interval (or window) that was initially specified, an inter-point interval must be defined. In cases in which exactly the same inter-point interval is applied to all windows and all files, the initial inter-point interval will be applied to each window unless the user specifies otherwise.

EXAMPLE OF PROGRAM INPUT-OUTPUT

The averaged EP waveforms in Figures 1 and 2 (data files DEMO1 and DEMO2) were recorded and plotted using the system described by Makasare et al. The average of the 50 data points

recorded prior to stimulus onset form a baseline from which peak deviations will be calculated.

The waveforms in the left-hand portion of Figure 1 were taken from a sleep study carried out in our laboratory. A multi-channel electrode placement was employed although only four of these channels were scored for purposes of illustration. In the left-hand portion of the figure, waveforms from midline frontal, central and parietal (Fz, Cz and Pz) and the left temporal (T3) regions are plotted. The right-hand portion is an enlargement of the Cz recording. The large amplitude negative-positive deflection is the so-called, K-complex often apparent to significant stimuli within sleep. The waveforms in Figure 1 are the average of 5 stimulus presentations. The total sweep time was 1800 ms, consisting of a 300 ms pre-stimulus interval and a 1500 ms post-stimulus interval. The sweep was based on 300 points (i.e., an sampling rate of 6 ms was employed).

The waveforms in Figure 2 are taken from a study of the contingent negative variation (CNV). An initial warning stimulus (S1) is followed 1.4 s later by a second stimulus (S2). S2 was either a low or a high pitched tone, the subject being instructed to press a button if it were high-pitched and to refrain from responding if it were low-pitched. (This is the familiar Go-NoGo paradigm often employed in studies of the CNV). Electrodes were placed at Fz, Cz and Pz. Also illustrated is the electro-oculogram (EOG) channel, used for the detection of eye movement artifact. A 2400 ms sweep was employed, the first 400 ms pre-stimulus period

being used to form a baseline. The EEG was therefore sampled every 8 ms. As may be observed, distinctive negative-positive deflections are visible following the presentation of S1 and S2. Between S1 and S2, a slow, long-lasting negative shift is evident. This is the CNV.

----- Insert Figures 1 and 2 about here -----

The data for Figures 1 and 2 were contained in files DEMO1 and DEMO2 respectively. For purposes of illustration, DEMO1 and DEMO2 were scored "simultaneously" (i.e., in the same session). Seven windows were established. In most instances, this would usually imply that 7 different time intervals (involving 7 different components) were selected for scoring. In this example, the same time interval (240-720 ms) was examined in windows 1 to 4 to score the prominent negative component in Figure 1 and a 780-1080 ms interval for the prominent positive component. Windows 6 and 7 were established to score DEMO2. Different scoring methods and options were applied to these windows. The various program prompts and input/output are contained in the appendices.

In Appendix 1, the user is asked to supply the names of the files to be scored. They are then asked for the number of stimuli to be scored (the upper limit is 4). Even if a file contains evoked potential data for four stimuli, not all need be scored. Therefore, when fewer than four stimuli are selected (as in the present example), the user must define specifically which they

wish to be scored. In this case, to the prompt " 1 " (i.e., what is the number of the first stimulus to be scored?), the user entered "1" (i.e., stimulus number 1 is to be scored in files DEMO1 and DEMO2). A possible 8 channels could be scored. Only three were selected for analysis. These were channels 2, 3 and 4 (i.e., channel 1 in Figures 1 and 2 will not be scored). Finally, the number of sub-intervals or windows that are to be scored is entered as "7" for this example.

In Appendices, 1.2 and 1.3, the various information required for the scoring of each of these seven windows is entered. As mentioned, the same 240 to 720 ms period was selected for windows 1 to 4 for the scoring of the negative peaks in Figure 1. An interval extending from 780 to 1080 ms was used for the scoring of the positive peak. Only DEMO 1 matches the 6000 ms point-interval that is entered and thus only DEMO1 will be scored with these sub-intervals. In the first and second windows, a reference channel analysis (RCA) is selected. Channel 2 (Cz) is selected as the reference channel. The "Name of Waveform" prompt is employed to provide a label for each of the selected windows (see output in Appendices 1.2.1). The only difference between the first and second windows is that a 30% noise-to-signal percentage was selected for the second window while none was selected for the first. A separate channel analysis (SCA) was used in Windows 3, 4 and 5. In Windows 3 and 5, no correction of background noise was made, while in Window 4, a 30% noise-to-signal percentage was again entered. In Windows 1 to 4, the maximum negative peak within the

interval was sought while in Window 5, the maximum positive peak was sought.

The output for Windows 1 to 5 is presented in Appendix 1.2.1. The first RCA analysis identified the maximum negative peak in the second channel at a latency of 588 ms (indicated by a dashed line in Figure 1). At this latency, its amplitude measured -86, -69 and -66 uV at Cz, Pz and T3 respectively. Whether this is truly representative of the overall large negative waveform is debatable. Several smaller negative peaks can be observed in the same latency range. Which of these small negative peaks is the actual "signal"? In the absence of other information, the question probably cannot be answered. However, an estimate of the true signal can be made. In the second window, a 30% noise-to-signal percentage was employed. The program searched to the left and right of the 588 ms peak maximum until a 30% decrement in the Cz amplitude (i.e. a decrement of approximately 25 uV) was detected. The 30% limits are indicated in the enlargement of the Cz waveform. The average of data points in this new sub-interval was -78, -58 and -52 uV at the three electrode sites. The mid-point of this sub-interval occurred at 564 ms. In Window 3, an SCA analysis was employed. The maximum peaks in channels 3 and 4 (Pz and T3) do not correspond to those detected for Cz. A triangle is used to identify these peaks in Figure 1. Note that the peak latency for these sites shifts by approximately 80-90 msec compared to the first window, although their amplitude remains approximately the same. When a 30% noise-to-signal correction procedure is employed

(Window 4), the mid-point latency is much closer to that observed in the reference channel analysis (Window 2). The large positive peak was found to be maximum at 984, 918 and 954 ms at Cz, Pz and T3 respectively in the SCA when no correction for background noise was employed (Window 5).

Windows 6 and 7 (Appendix 1.3) were used for the scoring of the CNV data. These are probably best scored using data pointy analysis (DPA). In Window 6, the data points between 300 and 540 ms were averaged while in Window 7, a 660 to 990 ms interval was selected. The starting point in Window 6 overlaps a positive component of the evoked potential to the first stimulus (S1). In this instance, the use of DPA is of dubious value. For both windows, the operator asked that the amplitude of all data points used to calculate the average be printed. The sub-intervals are illustrated in Figure 2 by dashed lines. Appendix 1.3.2 provides the output of these analyses. The average of channels 2, 3 and 4 (Fz, Cz and Pz) were +0.06, -2.43 and +0.07 respectively for the 300-900 ms interval and -7.13, -9.76 and -4.87 respectively for the 660 to 900 ms interval.

OVERVIEW

A comparison of computer and human scoring of evoked potential waveforms indicated that the automatic routines are quite reliable. The computer analysis is, however, not infallible and should be accompanied by a visual inspection of the plotted waveforms. In

general, when the components of an evoked waveform are clearly defined (i.e: when the signal-to-noise ratio is high), few problems are encountered. By contrast, when there is considerable background noise, inappropriate peaks may be identified, depending on the scoring method and options selected. In such situations, "eye-ball" scoring is probably no more reliable providing the human does not "smooth" the waveforms. The "Peak Percentage" routine can be applied to noisy waveforms with some degree of success. Nevertheless, it is recommended that such signals be digitally filtered prior to submission for automatic scoring. A problem also arises when the true "component" under consideration appears outside of the user-defined window. In these cases, the human scorer often "bends" the rules. The computer is not as flexible. On the other hand, several different windows of varying widths can be defined to score the same component, thereby increasing the likelihood of detecting it. Of course, false positives will ensue if the window is too wide. The fact that this program will process up to 200 files without requiring any user intervention affords a considerable reduction in time that would otherwise have been allocated to performing a tedious and repetitive task.

Availability of Program:

A listing of the program is available at no charge from from the authors. Upon request, a copy can be made on 5 1/4 inch diskette.

ACKNOWLEDGEMENTS

A number of colleagues have assisted in the development of the various computer routines and provided test data. In particular, we acknowledge the contributions of Nancy Noldy-Cullum and Braxton Suffield. Madan Makasare provided invaluable assistance in the understanding of the Cromemco microcomputer and the many programs he has written for it. This research was supported by the Natural Sciences and Engineering Research Council (NSERC) and the Medical Research Council (MRC) of Canada. IB was supported by a doctoral scholarship from NSERC and DDE by a doctoral scholarship from the MRC.

REFERENCES

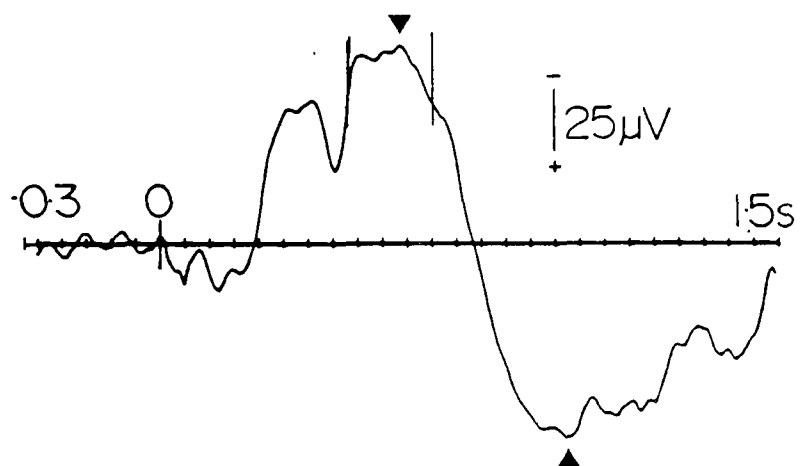
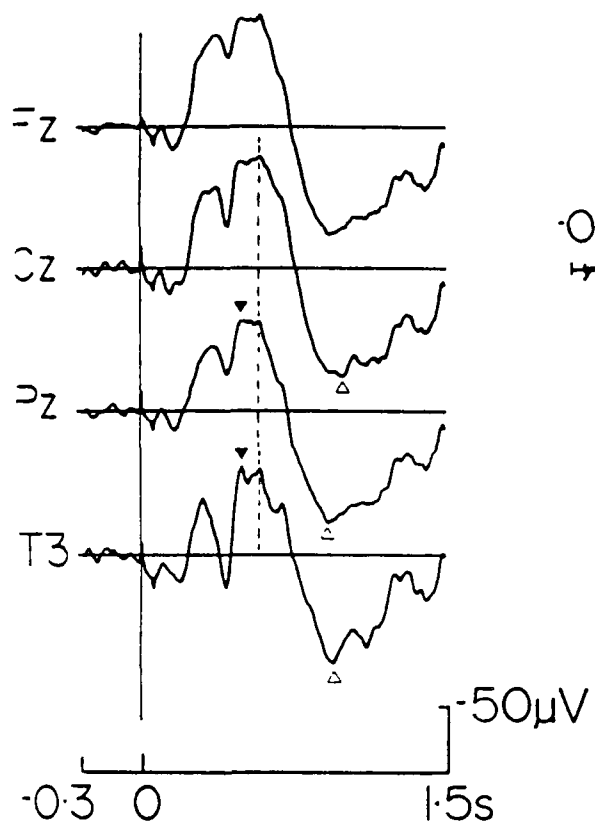
- Coles, M.G.H, Gratton, G., Kramer, A.F. and Miller, G.A. (in press) Principles of signal acquisition. In M.G.H. Coles, E. Donchin and S.W. Porges (Eds.) Psychophysiology: Systems, Processes and Applications. Guilford: New York.
- Donchin, E. and Heffley, E.F. (1978) Multivariate analysis of event-related potential data: A tutorial review. In D. Otto (Ed.) Multidisciplinary Perspectives Event-Related Brain Potential Research, (EPA-600/9-77-043). U.S. Government Printing Service: Washington, D.C., pp. 555-572.
- Fabiani, M., Gratton, G., Karis, D. and Donchin, E. The definition identification, and reliability of the P300 component of the event-related brain potential. (in press) In P.K. Ackles, J.R. Jennings and M.G.H. Coles (Eds.) Advances in Psychophysiology, Volume 2. JAI Press: Greenwich, CT.
- Makasare, M., Campbell, K.B., Stelmack, R.M. and Knott, V. (1985) A microcomputer system for the evoked potential laboratory. Psychophysiology, 22: 586,
- Picton, T.W. and Stuss, D. (1980) The component structure of the human event-related potentials. In H.H. Kornhuber and L. Deecke (Eds.). Motivation, Motor and Sensory Processes of the Brain, Progress in Brain Research (Vol 54), Elsevier: Amsterdam, pp. 17-49.

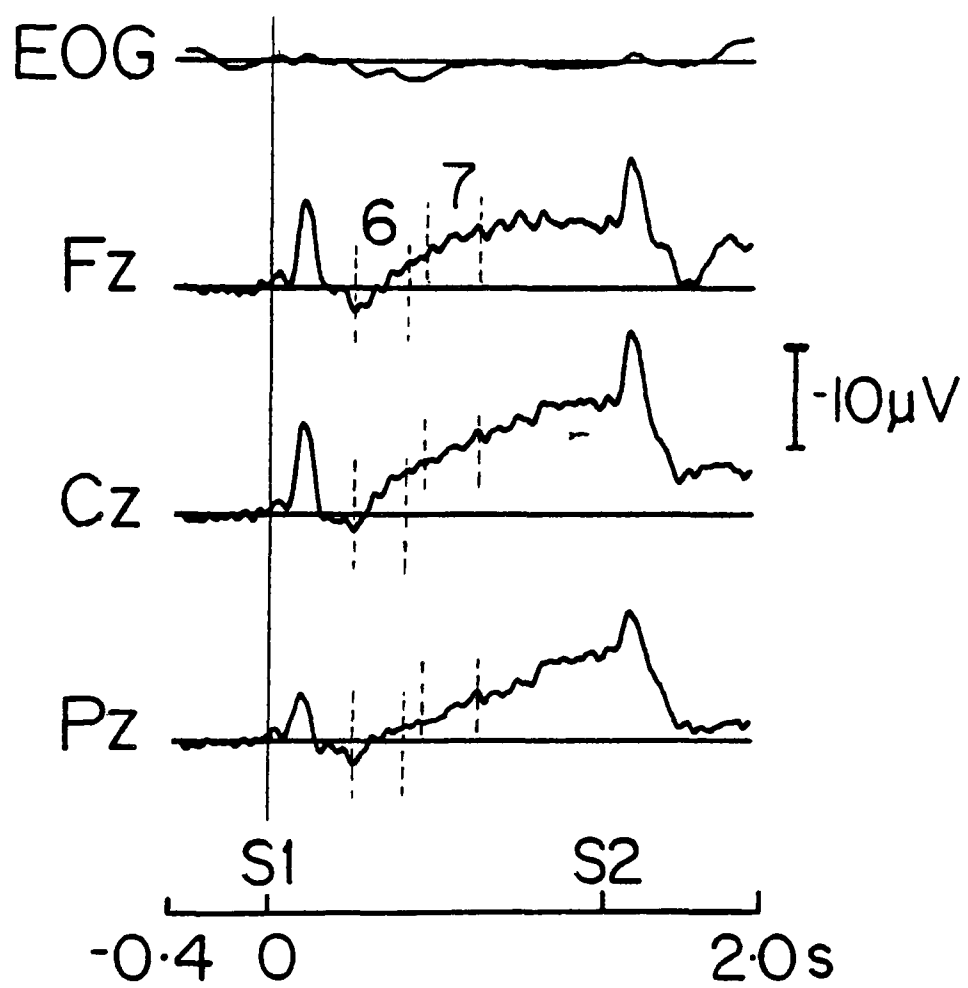
FIGURE LEGENDS

Figure 1 - Waveforms used for the scoring of file DEMO1. The large negative-positive deflection is a K-complex, occurring in a sleeping subject. Channels 2, 3 and 4 (Cz, Pz and T3) were arbitrarily chosen for scoring. A number of small deflections can be seen "riding on" the large negative-going wave occurring between 500 and 600 ms post-stimulus. In the example, a reference channel analysis (RCA) was performed, Cz being chosen as the reference channel. The right-hand portion of this figure is an enlargement of this channel. The inverted triangle in the enlargement indicates when the maximum negative peak was detected (i.e., 588 ms post-stimulus). At this latency (indicated by dashed lines in the left-hand portion), the amplitude at Pz and T3 is computed. However, as indicated in the third, separate channel analysis (SCA), the maximum negative peaks (indicated by the solid, inverted triangle) do not actually occur at the maximum peak latency of Cz. In the second analysis, a noise correction routine was applied to the RCA and in the fourth to the SCA. The solid bars in the right-hand portion of the figure indicate when the amplitude of the maximum peak (at 588 ms) has declined by 30%. The mid-point of this interval (564 ms) acts as the latency of the negative peak. The mean of all of all the data points in this interval becomes the amplitude of the peak. The open triangles indicate the maximum positive peak that was detected in the fifth analysis. As is apparent from the differing latencies for each

channel, an SCA procedure was employed.

Figure 2 - Waveforms used for the scoring of DEM02. The first channel was used for the detection of eye movement artifact and was not scored. Between S1 and S2, a negative-going slow wave (the "CNV") is apparent. Data points in the 300 to 540 ms and 660 to 900 ms interval were averaged (DPA routine). The intervals are indicated by dashed lines at each of the three electrode placements.





APPENDIX 1.00

EP Scoring Routine : Version 3.0

=====

by Ian Bell

U of Ottawa

Press <CR> to start, <ESC> to stop

(screen cleared)

Enter the name(s) of file(s)....max=200

eg: A:FILENAME.EXT

1 Filename---> DEMO1 Another? (Y/N) Y

2 Filename---> DEMO2 Another? (Y/N) N

(screen cleared)

Number of stimuli to score? (1-4) 1

1 ? 1

C)ontinue or R)eset values : C

(screen cleared)

Analyze all 8 channels? (Y/N) N

Number of channels to analyze? 3

Select from channels 1-8

1 ? 2

2 ? 3

3 ? 4

C)ontinue or R)eset values : C

(screen cleared)

Number of Windows? (max=10) 7

(screen cleared)

WINDOW 1

```

-----
Select Scoring Method :
  A: Reference Channel Analysis
  B: Separate Channel Analysis
  C: Data Point Averaging
->A

Channels to be scored : 2 3 4

Reference Channel..... 2
Name of Waveform..... RCA-N/S%=0
Start (in msec)..... 240
End (in msec)..... 720
Peak Percentage = 10% (Y/N)..... N
  Desired Percentage (0-100)..... 0
Valence of peak (N=neg, P=pos)..... N
Do you know Point Interval? (Y/N).... Y
  Point Interval (in microseconds) : 6000

C)ontinue or R)eset parameters : C

                          (screen cleared)

```

WINDOW 2

```

-----
Select Scoring Method :
  A: Reference Channel Analysis
  B: Separate Channel Analysis
  C: Data Point Averaging
->A

Channels to be scored : 2 3 4

Reference Channel..... 2
Name of Waveform..... RCA-N/S%=30
Start (in msec)..... 240
End (in msec)..... 720
Peak Percentage = 10% (Y/N)..... N
  Desired Percentage (0-100)..... 30
Valence of peak (N=neg, P=pos)..... N
Do you know Point Interval? (Y/N).... Y
  Point Interval (in microseconds) : 6000

C)ontinue or R)eset parameters : C

                          (screen cleared)

```

WINDOW 3

```

-----
Select Scoring Method :
  A: Reference Channel Analysis
  B: Separate Channel Analysis
  C: Data Point Averaging
->B

Name of Waveform..... SCA-N/S%=0
Start (in msec)..... 240
End (in msec)..... 720
Peak Percentage = 10% (Y/N)..... N
  Desired Percentage (0-100)..... 0
Valence of peak (N=neg, P=pos)..... N
Do you know Point Interval? (Y/N).... Y
  Point Interval (in microseconds) : 6000

C)ontinue or R)eset parameters : C

                          (screen cleared)

```

WINDOW 4

```

-----
Select Scoring Method :
  A: Reference Channel Analysis
  B: Separate Channel Analysis
  C: Data Point Averaging
->B

Name of Waveform..... SCA-N/S%=30
Start (in msec)..... 240
End (in msec)..... 720
Peak Percentage = 10% (Y/N)..... N
  Desired Percentage (0-100)..... 30
Valence of peak (N=neg, P=pos)..... N
Do you know Point Interval? (Y/N).... Y
  Point Interval (in microseconds) : 6000

C)ontinue or R)eset parameters : C

                          (screen cleared)

```

WINDOW 5

```

-----
Select Scoring Method :
  A: Reference Channel Analysis
  B: Separate Channel Analysis
  C: Data Point Averaging
->B

Name of Waveform..... SCA +PEAK
Start (in msec)..... 789
End (in msec)..... 1080
Peak Percentage = 10% (Y/N)..... N
  Desired Percentage (0-100)..... 0
Valence of peak (N=neg, P=pos)..... P
Do you know Point Interval? (Y/N).... Y
  Point Interval (in microseconds) : 6000

C)ontinue or R)eset parameters : C

```

APPENDIX 1.2.1

1.2 Data for file DEM01

Condition : K-COMPLEX IN SLEEP
Name : CU
Date : 85-11-23
Sweep Time : 1800 msec
Pt Interval: 6000 microsec
No. Stim. : 1
No. Chan. : 8

WINDOW	LABEL	START	END	P%	VAL	REF
1	RCA-N/S%=0	240	720	0	N	2
2	RCA-N/S%=30	240	720	30	N	2
3	SCA-N/S%=0	240	720	0	N	NONE
4	SCA=N/S%=30	240	720	30	N	NONE
5	SCA +PEAK	780	1080	0	P	NONE
6	DPA 1	300	540		D.P.A	
7	DPA 2	660	900		D.P.A	

STIMULUS	WINDOW	CHANNEL	PEAK	LATENCY	AMPLITUDE
1	1	2	NEG	588	- 86.63
1	1	3	NEG	588	- 69.34
1	1	4	NEG	588	- 66.68
1	2	2	NEG	564	- 77.72
1	2	3	NEG	564	- 57.77
1	2	4	NEG	564	- 51.97
1	3	2	NEG	588	- 86.63
1	3	3	NEG	510	- 69.68
1	3	4	NEG	498	- 68.34
1	4	2	NEG	564	- 77.72
1	4	3	NEG	546	- 63.80
1	4	4	NEG	540	- 59.30
1	5	2	POS	984	- 82.59
1	5	3	POS	918	- 85.33
1	5	4	POS	954	- 81.73
1	6	Window Point Interval = 8000			
1	7	Window Point Interval = 8000			

APPENDIX 1.3

WINDOW 6

Select Scoring Method :

A: Reference Channel Analysis

B: Separate Channel Analysis

C: Data Point Averaging

->C

Print values used to calculate average? (Y/N)...: Y

Name of Waveform.....: DPA 1

Start (in msec).....: 300

End (in msec).....: 540

Do you know Point Interval? (Y/N)...: Y

Point Interval (in microseconds) : 8000

C)ontinue or R)eset parameters : C

(screen cleared)

WINDOW 7

Select Scoring Method :

A: Reference Channel Analysis

B: Separate Channel Analysis

C: Data Point Averaging

->C

Print values used to calculate average? (Y/N)...: Y

Name of Waveform.....: DPA 2

Start (in msec).....: 660

End (in msec).....: 990

Do you know Point Interval? (Y/N)...: Y

Point Interval (in microseconds) : 8000

C)ontinue or R)eset parameters : C

Reset Window Values (Y/N) : N

...Accessing scoring routine....

APPENDIX 1.3.1

2.2 Data for file DEMO2

Condition : CNV STUDY

Name : DM

Date : 86-02-17

Sweep Time : 2400 msec

Pt Interval: 8000 microsec

No. Stim. : 4

No. Chan. : 6

WINDOW	LABEL	START	END	P%	VAL	REF
1	RCA-N/S%=0	240	720	0	N	2
2	RCA-N/S%=30	240	720	30	N	2
3	SCA-N/S%=0	240	720	0	N	NONE
4	SCA-N/S%=30	240	720	30	N	NONE
5	SCA +PEAK	780	1080	0	P	NONE
6	DPA 1	300	540		D.P.A	
7	DPA 2	660	900		D.P.A	

STIMULUS WINDOW CHANNEL PEAK LATENCY AMPLITUDE

1	1	Window Point Interval = 6000					
1	2	Window Point Interval = 6000					
1	3	Window Point Interval = 6000					
1	4	Window Point Interval = 6000					
1	5	Window Point Interval = 6000					
1	6	2	AVERAGE=	0.06			
1)	2.95	2)	3.25	3)	3.44	4)	3.54
5)	2.66	6)	1.98				
7)	2.07	8)	2.17	9)	2.47	10)	2.52
11)	2.07	12)	1.39				
13)	0.22	14)	0.56	15)	0.95	16)	0.27
17)	0.22	18)	0.61				
19)	0.22	20)	0.37	21)	1.74	22)	2.52
23)	3.01	24)	2.42				
25)	2.13	26)	1.83	27)	2.03	28)	2.22
29)	2.81	30)	3.30				
31)	3.69						
1	6	3	AVERAGE=	- 2.43			
1)	1.71	2)	1.90	3)	2.30	4)	2.49
5)	1.71	6)	1.12				
7)	0.73	8)	0.24	9)	0.15	10)	0.64
11)	0.73	12)	1.42				
13)	2.69	14)	3.66	15)	3.57	16)	2.98
17)	2.49	18)	2.59				
19)	2.98	20)	3.66	21)	4.54	22)	5.33
23)	5.91	24)	5.62				
25)	5.33	26)	5.03	27)	5.13	28)	5.42
29)	5.72	30)	5.81				
31)	6.20						
1	6	4	AVERAGE=	0.07			
1)	1.86	2)	2.54	3)	3.13	4)	3.71
5)	3.22	6)	2.83				
7)	2.34	8)	1.66	9)	1.17	10)	1.07
11)	0.98	12)	0.49				
13)	0.59	14)	1.37	15)	0.98	16)	0.39
17)	0.00	18)	0.20				
19)	0.39	20)	0.59	21)	1.27	22)	1.86
23)	2.15	24)	1.76				
25)	1.17	26)	1.08	27)	1.37	28)	1.86
29)	2.05	30)	1.86				
31)	1.95						
1	7	2	AVERAGE=	- 7.13			
1)	5.84	2)	4.96	3)	5.06	4)	5.25
5)	5.94	6)	6.43				
7)	6.72	8)	7.11	9)	7.89	10)	7.40
11)	7.31	12)	7.70				
13)	7.60	14)	7.01	15)	6.62	16)	6.62
17)	6.82	18)	7.21				
19)	7.50	20)	7.89	21)	7.40	22)	8.18
23)	8.77	24)	9.16				
25)	8.28	26)	7.79	27)	7.21	28)	6.72
29)	6.43	30)	7.50				
31)	8.48						
1	7	3	AVERAGE=	- 9.76			
1)	7.77	2)	7.48	3)	7.48	4)	7.77
5)	8.45	6)	8.84				
7)	8.84	8)	8.94	9)	9.72	10)	9.53
11)	9.53	12)	9.82				
13)	9.72	14)	9.43	15)	9.33	16)	9.14
17)	9.14	18)	9.33				
19)	10.02	20)	10.41	21)	10.41	22)	10.89
23)	11.77	24)	12.26				
25)	11.87	26)	11.38	27)	10.50	28)	9.82
29)	9.92	30)	10.99				
31)	12.07						
1	7	4	AVERAGE=	- 4.87			
1)	2.93	2)	2.83	3)	2.93	4)	3.03
5)	3.32	6)	3.42				
7)	3.32	8)	3.71	9)	4.59	10)	4.59
11)	4.69	12)	4.98				
13)	4.98	14)	5.18	15)	5.18	16)	4.98
17)	4.69	18)	4.59				
19)	5.08	20)	5.47	21)	5.57	22)	6.06
23)	6.64	24)	6.94				
25)	6.94	26)	6.74	27)	5.86	28)	4.89
29)	4.59	30)	5.57				
31)	6.74						