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Antecedents and Consequences of the Evoked K-Complex

by

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Abstract

Three experiments were run in order to determine the antecedents and consequences of the evoked K-Complex. In all three experiments, a train of auditory stimuli was presented during stages 2, 3 and 4 of sleep. In experiment 1, the intensity of the stimulus (80 and 60 dB SPL), its rise-and-fall time (2 and 20 ms) and its tonal frequency (500, 1000 and 2000 Hz) were manipulated. The evoked K-Complex consisted of two different negative components peaking at approximately 350 ("N350") and 550 ("N550") ms, respectively, and followed by a positive component peaking at approximately 900 ("P900") ms. K-Complexes occurred more often with high intensity, fast rise-and-fall time stimuli. When a K-Complex was evoked, the amplitude and latency of the different components remained invariant regardless of the intensity, rise-and-fall or tonal frequency of the stimulus. The K-Complex therefore appears to be an all-or-none phenomenon. On trials on which a K-complex could not be elicited, N350 was still visible although much attenuated. On these trials, its amplitude was further reduced when stimulus intensity was lowered. N350 might need to reach a certain critical threshold before the much larger N550-P900 complex is elicited.

Experiment 2 examined the effects of rate of presentation on the evoked K-Complex. In different conditions, brief duration tone pips were presented every 5, 10 or 30 sec. K-Complexes were elicited most often when the rate of stimulus presentation was

slowest (i.e., every 30 sec) compared to when it was faster (i.e., every 5 or 10 sec). When a K-Complex was evoked, the amplitudes of N350 and N550 were greater with the 30 than the 10 or 5 sec rate of stimulus presentation. A micro-analysis was carried out when 3 consecutive K-Complexes were elicited. With the faster rates of presentation, N350 and N550 following the second and third occurrence of the K-Complex were significantly attenuated compared to the first occurrence. There was no difference in N350 and N550 amplitudes among the 3 consecutive occurrences during the Slow condition. The decay in amplitude over consecutive occurrences of the K-Complex was interpreted as due to either habituation or refractory processes.

Experiment 3 was designed to determine the function of the K-Complex. It has been considered to reflect either an arousal or a sleep protector mechanism. A spectral analysis of the EEG prior to and following the presentation of a stimulus was compared on trials on which a K-Complex was and was not elicited. Tone pips were presented every 20 sec during non-REM sleep. FFTs were computed on the EEG prior to and following stimulus onset. In the absence of a K-Complex, a small but significant power elevation following stimulus onset was apparent during Slow Wave Sleep. There were no changes in EEG activity when a K-Complex was elicited. The K-Complex therefore appears to prevent arousal that might otherwise occur to external stimuli.

Résumé

Trois expériences furent réalisées afin de déterminer les antécédents et les conséquences du Complexe-K évoqué. Dans ces trois expériences, un train de stimuli auditifs fut présenté dans les stades de sommeil 2, 3 et 4. Dans l'expérience 1, l'intensité du stimulus (60 vs 80 dB), son temps de montée (2 vs 20 msec) et sa fréquence (500, 1000 ou 2000 Hz) furent manipulés. Le Complexe-K évoqué consistait en deux composantes négatives différentes apparaissant respectivement vers 350 ("N350") et 550 ("N550") ms et suivis d'une composante positive apparaissant vers 900 ("P900") ms. Les Complexes-K étaient plus souvent évoqués avec des stimuli d'intensité élevée et de temps de montée rapide. Quand un Complexe-K était évoqué, l'amplitude et la latence des différentes composantes demeuraient invariables malgré les manipulations dans l'intensité, le temps de montée et la fréquence du stimulus. Le Complexe-K semblait donc obéir au phénomène du "tout-ou-rien". Durant les essais où un Complexe-K ne pouvait être identifié, N350 était toujours visible malgré une amplitude réduite. Durant ces essais, son amplitude était plus fortement réduite avec une diminution dans l'intensité du stimulus. N350 doit peut-être atteindre un seuil critique de façon à ce que le complexe N550-P900 soit subséquemment évoqué.

L'expérience 2 examinait les effets d'intervalles inter-stimuli (IIS) différents sur le Complexe-K évoqué. Dans des conditions différentes, des tons de courte durée étaient présentés toutes les 5, 10 ou 30 sec. Les Complexes-K

apparaissaient plus fréquemment lorsque l'IIS était plus lent (30 sec) que lorsqu'il était plus rapide (5 ou 10 sec). Quand un Complexe-K était évoqué, l'amplitude de N350 et N550 étaient plus élevées avec un IIS de 30 sec qu'avec un IIS de 5 ou 10 sec. Une micro-analyse fut également effectuée lorsque 3 Complexes-K consécutifs étaient évoqués. Avec de courts IIS, N350 et N550 étaient significativement atténués lors de la 2^{e} et 3^{e} apparition comparativement à la première apparition d'un Complexe-K. Il n'y avait pas de différences dans l'amplitude de N350 et N550 lorsque l'IIS était long. La diminution dans l'amplitude des composantes fut interprétée comme étant dûe au phénomène d'habituation ou de période réfractaire.

L'expérience 3 fut effectuée afin de déterminer la fonction du Complexe-K. Il a été considéré comme étant soit un mécanisme d'éveil ou de protection du sommeil. Une analyse spectrale du EEG avant et après la présentation d'un ton auditif fut comparée pour les essais contenant et ne contenant pas de Complexes-K. Les tons étaient présentés à chaque 20 sec. Les analyses spectrales (Transformations de Fourrier, "FFTs") furent calculées avant et après la présentation des tons. Lorsque le Complexe-K était absent, une élévation minime mais significative dans la puissance après la présentation du ton était apparente dans les stades de sommeil 3 et 4. Il n'y avait pas de changement dans le EEG lorsqu'un Complexe-K était présent. Le Complexe-K semble donc prévenir l'éveil qui autrement apparaîtrait aux stimuli externes.

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Curriculum Studiorum

Celyne Bastien was born in Buckingham, Québec on July 3rd, 1965. She completed her B.A. in Psychology at the University of Ottawa in 1989. During her doctorate, she published a series of articles and presented papers at various conferences.

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Organizational Note

This dissertation consists of 5 chapters. Chapter 1 presents the Introduction, the literature review and develops the rationale for the three experiments that follow. Chapters 2, 3 and 4 present the results from these experiments. They are presented in article format. As such, separate Introduction, Methods, Results and Discussion sections are presented in each. Chapter 5 presents a general discussion and integration of the three experiments. Overall conclusions are provided. Each of the chapters is written in the format for the journal to which the article has been (or will be) sent. Chapter 2 has been published in Sleep. Chapter 3 is "in press" in the Journal of Sleep Research. Chapters 4 and the integration of 1 and 5 will also be sent to this journal. References are presented at the end of the thesis rather than at the end of each chapter to avoid redundancy.

Chapter 1

Review of the literature

Introduction

For almost a century, researchers have sacrificed their own sleep to monitor other people's sleep (Dement, 1976; Webb, 1975). In a whole night of sleep, 90 minute cycles (as described by Rechtschaffen and Kales, 1968) will comprise different stages of sleep: 1, 2, 3, 4 and REM. Stages 1 through 4 are often grouped together as non-REM (or "NREM"). The stages of sleep are defined by differing patterns of EEG, EOG and EMG activity. Stage 1 is a transitional phase between wakefulness and sleep. Relatively low voltage, mixed 2 to 7 Hz frequency waves characterize the EEG. Slow rolling eye movements are also observed during stage 1, particularly at sleep onset. The presence of transient sleep spindles and K-Complexes mark the onset of stage 2. A sleep spindle consists of 12 to 14 Hz highly rhythmic EEG activity that lasts at least 0.5 sec. A K-Complex is a high amplitude (200 - 500 μV) EEG waveform having a well-delineated negative component immediately followed by a positive deflection. Mixed frequency waves (1 - 3 Hz) and some delta waves are also present in the EEG. A delta wave has an amplitude greater than 75 μV and a frequency from 0.5 to 2.0 Hz. The occurrence of a large proportion of delta waves in the EEG defines stages 3 and 4. Stage 3 has from 20 to 50% delta while stage 4 has greater than 50% delta activity. Stages 3 and 4 are collectively referred to

as Slow Wave Sleep (SWS). Eye-movement activity is negligible during stages 2, 3 and 4. Low EMG levels are typical of stages 1, 2, 3 and 4. The EEG pattern during REM sleep is similar to that of stage 1. However, "sawtooth" waves are frequently present. This stage of sleep is characterized by rapid, conjugate eye movements, hence the name "REM" sleep. Tonic EMG is at its lowest during REM sleep.

The subject of this thesis is the K-Complex. Its morphology and functional significance will be examined. Loomis, Harvey and Hobart (1939) were the first to report that the presentation of an external stimulus to the sleeping subject could elicit a very large amplitude waveform which they called the "K-Complex". In the same year, Davis, Davis, Loomis, Harvey and Hobart reported that the K-Complex might also appear spontaneously without any apparent external stimulation. The reason the response was named the "K"-Complex remains somewhat of a historical mystery. H. Davis (personal communication to Ehrhart, 1974) has indicated that the "K" of the K-Complex had no particular significance. The label "Complex" was given because of mixed fast and slow waves which composed the waveform, and the fact that the two "components" (fast and slow) may vary independently from one other.

A summary of studies that have examined the evoked K-Complex (that is, those elicited by some external stimulus) is presented in Table 1. Controversial issues, as well as areas in which common agreement has been reached, will be discussed in

this review. Amongst the major issues are: a) the morphology of the K-Complex (does it consist of 2, 3 or more different components or should it be considered a single unit entity?); b) its topographical distribution (what is the voltage distribution of the various components of the K-Complex across the scalp?); c) the notion that the K-Complex may be an all-or-none phenomenon (does it vary with changes in the stimulus characteristics?); and, finally, d) its functional significance (does it serve to inhibit or promote sleep?). Other areas, such as its ontogenesis, its relationship with spindles and the influence of different pathologies will also be examined.

Morphology of the K-Complex

Davis et al. (1939) reported that the K-Complex consisted of at least a large negative-going followed by a positive-going wave. Despite the fact that at least two different waves were identified, early studies considered the K-Complex as a single entity. Independent functional significance for each of the waves was not considered.

In very young infants (< 2 years), the K-Complex is not well-formed. The initial (negative) and later (positive) waves are not sharp and not topographically delimited. Between the ages of 3 to 9, only the large negative wave can at times be observed. The division of the K-Complex into separate components does not occur before 16 years of age (Metcalf, Mondale and Butler, 1971).

Davis et al. (1939) noted that spindle activity was closely associated with K-Complexes. Roth, Shaw and Green (1956) considered spindle activity to be part of the K-Complex. Therefore, the K-Complex was thought to consist of three different components: a fast negative wave, a slow positive wave and a trailing sleep spindle. To be defined as a K-Complex, the isolated waveform had to be unusually large in amplitude (at least 100 μV although it often exceeded 200 μV). Roth et al. (1956) claimed that the voltage of the response influenced its form --the larger the K-Complex, the sharper were the waves. More recent studies have not supported this claim.

Oswald, Taylor and Treisman (1960) explored the influence of the psychological significance of the eliciting stimulus on the K-Complex. They used the same criteria as Roth et al. (1956) to define it. They noted, however, that the positive wave might appear in isolation from other components. They considered its appearance and functional role to be related to the K-Complex. Unlike Roth et al. (1956), Johnson and Lubin (1966) considered only the large amplitude negative-positive complex to be the K-Complex. Spindle activity was not required nor did they specify amplitude criteria.

A standard manual for the scoring of sleep recordings was adopted in 1968 (Rechtschaffen and Kales, 1968). In it, the spontaneous K-Complex was defined as a large amplitude (more than 75 μV) negative-positive waveform that may or may not be overlapped by spindle activity. Latency criteria were also

specified for the different waves. The negative wave had to occur between 300 and 700 msec and the positive wave had to occur at about 1000 msec following stimulus onset. Criteria for the definition of the evoked K-Complex were not provided. Most authors nevertheless employ similar criteria.

Halász, Pál and Rajna (1985) carried out an extensive study of the K-Complex. They concluded that the evoked K-Complex consisted of at least two independent peaks, a negative wave peaking at approximately 550 msec (hence "N550") and a positive wave peaking at approximately 900 msec (hence "P900"). There was, however, considerable within and between subject variability. They noted that the N550-P900 complex could be mono-, bi- or even polyphasic (thus having more than 2 waves). They also reported that it may or may not be followed by spindle activity. In a follow-up study, Ujszászi and Halász (1986) claimed that there were at least three different biphasic K-Complex forms: a N300-P400, a N300-P800 and a N600-P800 wave. Ujszászi and Halász (1988) distinguished two negative deflections: an earlier negative peak occurring at about 350 msec (thus "N350") followed immediately by the second large negative peak, "N600".

Paiva and Rosa (1991) recently proposed 6 different morphological variations of the isolated, spontaneous K-Complex: a) a clearly biphasic negative-positive event, with a sharp negative component; b) a biphasic K-Complex (negative-positive complex), with a double peak in the negative component; c) a K-

Complex with a single smoothed negative component (smoothing out the double negative peak) followed by a positive component; d) a predominantly monophasic positive wave; e) a polyphasic K-Complex; and, f) other shapes (such as an initial positive peak before the negative-positive complex). The extent to which such an all-encompassing system is affected by overlapping background noise is not clear. Single K-Complexes are, of course, embedded in the ongoing EEG. The background EEG in stage 2 can exceed 100 μV while in stage 4, it can be from 200 to 400 μV. It is quite possible that a portion of the apparent polyphasic activity might be due to summation with background EEG activity.

Few attempts have been made to compare the morphology of spontaneous and evoked K-Complexes. This may not be an easy task. In order to determine whether the K-Complex is a mono-, bi- or polyphasic waveform, a reference or "starting" point must be used. In the case of the evoked K-Complex, this is obviously the stimulus. In the case of the spontaneous K-Complex, there is no obvious event to which it can be time-locked.

K-Complexes and Spindles

Both K-Complexes and spindles can occur spontaneously without any apparent external stimulation during non-REM sleep. As mentioned, many authors consider the spindle to be an integral part of the K-Complex. Several (for example, Hongo, Kubota and Shimizu, 1963; Yamadori 1971; Johnson, Hanson and Bickford, 1976; Ehrhart, Ehrhart, Muzet, Sheiber and Naitoh, 1981; Roth et al.

1956; Sassin and Johnson, 1968; Raynal, Montplaisir and Dement, 1974; Jankel and Niedermeyer, 1985) postulate that spindles promote sleep while K-Complexes inhibit it. Church, Johnson and Seales (1978) examined K-Complexes that occurred simultaneously with sleep spindles and those that did not. They observed that sleep spindles did not inhibit the occurrence of evoked K-Complexes. They concluded that sleep spindles were excitatory events, an hypothesis previously suggested by Moruzzi, Brookhart, Niemer and Magoun (1950) and Herz (1965). On the other hand, Naitoh, Antony-Baas, Muzet and Ehrhart (1982) observed a decrease in the number of K-Complexes after the occurrence of sleep spindles, thus supporting the notion of an inhibitory function of the spindles. They also observed that a decrease in sleep spindles increased the probability of occurrence of spontaneous K-Complexes and vice versa. Ehrhart et al. (1981) noted that a spindle could occur before, during or after a K-Complex. Naitoh et al. (1982) subsequently observed that more than one sleep spindle (either prior to, during or/and after the K-Complex) could also occur in conjunction with the K-Complex. In general, however, K-Complexes occurred independently of spindles. When the two were observed, the spindle usually either preceded or followed the K-Complex. It was relatively rare to observe a spindle embedded in a K-Complex. The present evidence leans toward the notion that the K-Complex and spindle are relatively independent phenomena. The issue remains a topic of debate.

Ontogeny

Few laboratories have examined the K-Complex in early infancy. Metcalf et al. (1971) have provided the classical database. The spontaneous K-Complex cannot be identified before 6 months of age. Individual K-Complexes remain difficult to discern in the on-going activity in the first 2 years of life. This could be because of its widespread distribution over the scalp (mid-temporal, temporal and temporo-parietal). It manifests a progressive change (becoming more defined in morphology) until 2 years of age. Between 6 and 7 years of age, another maturation process begins. Changes in morphology (sharpening of the waves) continue to occur until 12 years of age.

It is only after the age of two that the topography of the K-Complex becomes less widespread tending to become maximal at the vertex. Between 14 and 16 years of age, K-Complexes are maximum at the vertex (Metcalf et al., 1971). No further changes in scalp distribution have been reported through early and middle adulthood. After 70 years of age, the peak amplitude of the K-Complex is largest over temporal rather than centro-frontal regions (Wauquier, 1991). This parallels changes seen in the topography of delta waves (Wauquier, 1991).

K-Complexes appear spontaneously in both NREM and REM sleep in 8-12 years old preadolescents and children (Pivik, personal communication). They can only be observed in non-REM in adults. They do not occur spontaneously and cannot be evoked in REM sleep

in adults or while the subject is awake. Between the ages of 3 and 9, spontaneous K-Complexes may appear at a rate of 3 per minute, while in young adults they can occur at a rate of 1 per min (Halász and Ujszászi, 1991). In the elderly (> 70 years), K-Complexes become less frequent (Wauquier, 1991). No gender differences in K-Complex incidence have been clearly established (Wauquier, 1991).

K-Complexes and Pathology

Many studies have examined K-Complexes in epilepsy (Vinoles and Fuster, 1956; Niedermeyer 1987, 1991). There is little doubt that K-Complexes are associated with paroxysmal bursts in generalized epilepsy and that possible relationships between K-Complexes and other forms of epileptic seizure disorder also exist (Niedermeyer, 1991). In focalized epilepsy, K-Complexes are highly asymmetrical in the "fovea" and the area of the epilepsy (Vinoles and Fuster, 1956).

Karacan, Williams, Bose, Hursch and Warson (1972) reported that K-Complexes were of poor quality in patients undergoing dialysis following kidney transplantation. In post-traumatic coma, Bergamasco, Bergamini and Doriguzzi (1968) noted a decrease in K-Complexes and sleep spindles even if a greater amount of stage 2 could be observed. In "alcoholic withdrawal syndrome", K-Complexes are infrequent or even absent and have an abnormal morphology (Johnson, Burdick and Smith, 1970). Zarcone, Gibson, Widrow, Linsenbardt, Dickerson, Smythe, Hoddes, Phillips and

Dement (1973) also observed a significant decrease in the number of K-Complexes in patients with alcoholic withdrawal syndrome.

In children suffering from enuresis, Gastaut, Batini, Broughton, Fressy and Tassinari (1965) found an increase in K-Complexes followed by a lighter stage of sleep about 20 sec to 3 min before micturation. Gastaut and Broughton (1965) also observed K-Complexes with primitive bladder constrictions in enuretic children. In sleep terrors, bursts of K-complexes are almost always present before awakening. K-Complexes are often observed in conjunction with tachycardia, a decrease in skin resistance, an increase in body movement and apnoea in adults (Gastaut and Broughton, 1965). A similar pattern can be identified in children (Gastaut et al., 1965). Finally, in bruxism and tooth-grinding, the beginning of an episode is often preceded by a K-Complex, alpha activity and random EEG activity (Reding, Zepelin, Robinson, Zimmerman and Smith, 1968; Satoh and Harada, 1971).

Topographical distribution

A method often used to distinguish among the components of an evoked potential is to compare their scalp topography. Variation in the voltage of electrical potentials across the scalp (topographical distribution) is often used as a proof of the independence of different components. Components whose scalp distribution is different must have different intra-cranial generators (Näätänen and Picton, 1987). Some early studies have

reported that the K-Complex (usually in referring to the large negative wave, although not always specified) was maximum in amplitude over central and temporal regions of the scalp (Davis et al., 1939; Loomis et al., 1939; Oswald et al., 1960). However, Roth et al. (1956) reported that "despite the peak reversal or voltage peak at or near the vertex, the K-Complex is extensively distributed and clearly seen in the occipital, temporal and frontal regions with bipolar or unipolar recording". They speculated that the widespreaded distribution of K-Complexes was a result of diffuse projection system to the cortex with probable participation of the thalamus. They also observed that "a voltage peak at some point in the mid-line is thus always demonstrable for the first (negative) and third (spindle) components of the K-Complex and occasionally for the second (positive)". Jurko and Andy (1978) used implanted electrodes to record a K-Complex in the medial thalamic region of a single patient. They concluded that a part of the diffuse reticular system and/or the anterior thalamus may be maximally involved in eliciting the K-Complex. Jurko and Andy also claimed that partially independent neurophysiological mechanisms may be involved for the sharp (negative) and slow components (positive) of the K-Complex and its spindle component, because they observed a latency difference and a different voltage distribution for these waves.

Davis et al. (1939) suggested that the slow component (latency around 900 msec) was a delayed generalized response of

the cortex to sensory stimulation. They proposed that there may be two distinctive types of slow components, one frontal and the other central. One system initially activates the central cortex and a second activates the frontal cortex. Both systems seem to share common control over a given area, and thus produces a typical mixed response. There has been little subsequent empirical support for these claims.

More than 50 years later, others have noted that the negative (N550) peak was more prominent at frontal sites (Ujszászi and Halász, 1988). An earlier negative peak (N350) seemed to be more centrally distributed than the N550 (Ujszászi and Halász, 1988). Paiva and Rosa (1991) found the largest number of K-Complexes (mainly the negative peak at 550 msec) to be in the frontal and central regions. The topographical distribution of the K-Complex depended on the morphology of the negative component (the topography of the K-complex would be defined according to the sharpeness of the negative wave at one site). Other topographical variances among N350 and/or P900 peaks were not considered.

Functional Significance of the K-Complex

Antecedents

The various conditions in which a K-Complex can be elicited serve as the building blocks for the development of a theory to explain its functional correlates. Once the effects of different stimulus parameters on the likelihood of occurrence or on the

morphology of the K-Complex are established, generalizations can be made that may lead to a theory about its functional significance. While the antecedents to the elicitation of a K-Complex can be used to infer functional significance, they do not in themselves constitute a theory.

Subjects/Individual differences

The number of subjects that have been tested have varied greatly among the different studies reported in Table 1. Some studies (Roth et al., 1956) have used as many as 95 subjects while others (Davis et al., 1939) have used as few as a single subject. Usually, sample sizes tend to be rather small (from 5 to 10 subjects). Subjects are not always screened for normal hearing, sleep disturbances or psychiatric/neurological history.

Johnson and Karpman (1968) claimed that the K-Complex was a very consistent and stable inter-night and intra-subject phenomenon. However, this issue has not received extensive study. Scott, Karle, Switzer, Hart, Corriere and Woldenberg (1978) reported that following a therapy session, the frequency of K-Complexes increased significantly throughout the night. It resulted in a much greater intra-night variability for each of their subjects. They also reported a great inter-night variability. As already mentioned, the frequency of occurrence of K-Complexes does vary with age.

Stages of sleep

The scoring of sleep records was somewhat arbitrary prior to the advent of the Rechtschaffen and Kales (1968) standardized sleep staging method. Loomis et al. (1939) derived 5 sleep stages that they labelled A to E: A) interrupted alpha: the normal waking 10/sec rhythm dominates the pattern; B) low voltage: the alpha rhythm is lost; C) spindles: short groups ("spindles") of 14 Hz waves appear and also random delta waves of 0.2 sec or more in duration; D) spindles plus random: both types of waves increase in voltage and the delta waves are of longer duration; and, E) random: the 14 Hz waves become inconspicuous, but delta waves continue to increase in voltage and wavelength. This classification was used for more than 15 years. Dement and Kleitman (1957) subsequently offered a classification in which REM sleep was added.

The K-Complex (spontaneous or evoked) was recorded in stages C, D and E of Loomis et al. (1939) (stages 2, 3 and 4 of the Rechtschaffen and Kales method). Oswald et al. (1960) claimed that the K-Complex disappeared in Stage 4 sleep. Weitzman and Kremen (1964), however, noted the occurrence of the K-Complex in stage 4. Subsequently, most researchers have agreed that K-Complexes did occur in Stage 4 but cautioned that they were often obscured by high amplitude delta activity common to this stage (Johnson and Lubin, 1966; Johnson, Townsend and Wilson, 1975; Johnson et al., 1976; Church et al., 1978; Pál, Simon and Halász, 1985; Ujszászi and Halász, 1986). In short, K-Complexes were most

likely present but could not always be observed. K-Complexes are therefore usually identified and measured in Stage 2.

Some studies (Davis et al., 1939; Oswald et al., 1960) have reported that the probability of occurrence of the K-Complex varied in the different stages of sleep. More K-Complexes can be identified in stage 2 than in stage 3 and 4 (but of course, this may be confounded by the fact that K-Complexes are difficult to observe in stages 3 and 4). Halász et al. (1985) observed more K-Complexes in ascending (moving from a deeper to a lighter stage of sleep) than descending (moving from a lighter to a deeper stage of sleep) slopes of stage 2 sleep cycles. They also observed that the frequency of K-Complexes decreases from sleep onset to morning awakening, and from cycle-to-cycle. K-Complexes were more frequently observed when stage 2 was followed by stage 3-4 than by stage REM. However, others note that a significantly larger number of K-Complexes occur in the 10 minute time period prior to REM sleep (Largo, Leittao, Rosa and Paiva, 1991; Halász, Rajna, Kundra, Vargha, Bologh and Kemeny, 1977). On the other hand, Paiva and Rosa (1991) have indicated that the frequency of occurrence of a spontaneous K-Complex does not vary among the stages or cycles of sleep. The number of K-Complexes markedly increases in the period prior to *any* stage transition (i.e., not just REM or when the transition is into a "deeper" stage of sleep). These discrepancies might be due to how the K-Complex was measured by the different authors. This problem will be discussed later.

The K-Complex does not occur spontaneously and cannot be evoked in REM sleep or during the waking state in adults. There does not seem to be an adequate explanation for its absence in REM.

Stimulus Characteristics

Davis et al. (1939) observed that the K-Complex can be evoked by different stimuli independently of their modality. Roth et al. (1956) also observed that the K-Complex could be generalized to different stimuli by delivering acoustic, visual, painful shock and tactile stimuli. Their results showed that the K-Complex remained morphologically invariant under the influence of the different stimuli but that it was easier to elicit with an auditory stimuli. Subsequent studies have almost always used auditory stimulation to evoke a K-Complex. This is because the experimenter can assure constancy of stimulus input to the sleeper's ear, something that cannot be assured using visual stimuli when eyes are closed. As shall be observed later in this review, the assumption of constancy of auditory input is, in fact, highly dubious.

There is much inconsistency in actual stimulus parameters. Many different stimuli have been employed to elicit the K-Complex. Tactile stimuli have consisted of needle, pressure and electrical shocks that were at times painful. Visual stimuli have been primarily mainly flashes. Auditory stimuli have been frequently employed, mainly tone-pips, clicks, noise -- airplane,

horns -- and taped names. Even when the same type of stimulus is employed across laboratories, the rate of stimulus presentation has varied from rapid (one or more per second) to very slow (from a stimulus every minute to every 15 minutes). Parameters such as intensity, frequency, duration and rise-and-fall time also vary widely from study to study. At times, stimulus parameters have not been stated.

Many different auditory stimuli having very different parameters (intensity, frequency, rise-and-fall time, duration, names) have been employed to elicit the K-Complex. Comparison across studies is therefore difficult. The accurate interpretation of the K-Complex requires a systematic step-by-step manipulation of each of the stimulus parameters. Certain of these parameters will be expected to affect the K-Complex while others will not.

Some studies do not mention how the auditory stimuli were transduced. In most studies, stimuli are presented through a loud speaker mounted above or beside the subject's head. The physical quality of the sound reaching the ear will vary depending on the head position. A better method of transduction is the earphone "insert", often the type used in portable cassette and compact disc players or a hearing-aid/ear mould system (Campbell, Bell and Deacon-Elliott, 1985; Campbell and Bartoli; 1986). These systems assure constancy of stimulus input in spite of changes in the subject's head position during the night.

The measurement of the K-Complex may also vary from study-to-study. Again, the K-Complex is difficult to observe in the ongoing EEG and might thus be difficult to score, especially if studies differ in the stages of sleep in which K-Complexes were observed.

Intensity

The intensity of the stimulus is the most likely parameter that would affect a response (Graham, 1979). Unfortunately, comparison across laboratories is difficult because of the wide range of stimuli and intensities that have been used. Intensity has ranged from 30 to 110 dB SPL but in the majority of studies a 60 to 80 dB SPL short duration tone-pip has been used. In some cases, intensity was not stated.

Johnson and Lubin (1966) did not observe any change in the rate of responding throughout the night as a function of variations in stimulus intensity. However, their stimuli however, varied only between 30 and 35 dB HL (approximately 45-50 dB SPL). Ehrhart et al. (1981) studied 4 different airplane noises having 4 different intensities (77, 80, 82 and 96 dB SPL). They reported no differences in the probability of eliciting a K-Complex as a function of stimulus intensity. Campbell et al. (1985) employed 4 different intensity tone-pips (50, 60, 70 and 80 dB SPL) and observed a higher probability of eliciting a K-Complex with higher intensities. Although the intensities employed in the Ehrhart et al. and Campbell et al. studies were

similar, the type of stimulus (meaningful aircraft noise vs pure tones) and their characteristics (long rise-and-fall times and duration versus short rise-and-fall times and duration) make a direct comparison difficult. Campbell et al. (1985) also reported that the amplitude of the averaged K-Complex (they used averaging techniques to remove background EEG "noise") varied directly with the intensity of the stimulus. This could, however, be an artifact of their averaging technique i.e., all trials were averaged, whether they elicited a K-Complex or not and since higher intensities elicited more K-Complexes, *on average* the amplitude of the K-Complex would appear to be larger to high than low intensities.

The effect of stimulus intensity on the K-Complex remains, perhaps somewhat surprisingly, largely unresolved. Stimulus intensity remains a critical parameter for testing the all-or-none hypothesis. If the K-Complex acts as an all-or-none response, its amplitude should remain constant in spite of variation in the intensity of the stimulus.

Rate of Presentation

Roth et al. (1956) were the first to study the influence of the inter-stimulus interval (ISI) on the evoked K-Complex. They reported that with ISIs longer than 3 sec, a K-Complex could be evoked on every trial in some, but not all, subjects. The K-Complex was not in its refractory period when the ISI was longer than 3 sec since continuous responding was observed to occur

without any observable decrease in the amplitude of the early and late waves. With an ISI shorter than 3 sec, K-Complexes occurred only intermittently. If the ISI was shorter than 1 sec, no K-Complexes could be elicited. The refractory period for elicitating the K-Complex was thus between 1 and 3 sec. In this case, the term "refractory period" is used in reference to the appearance of a K-Complex. Its actual amplitude -- critical for the definition of the term "refractory period" -- was not measured.

Oswald et al. (1960) did not find any significant difference in the probability of eliciting a K-Complex with ISIs that varied from 4 to 8 sec. However, a K-Complex was not elicited on every trial. Firth (1973) presented stimuli with either fixed (10, 20 or 30 sec) or random ISIs (varying from 8 to 12, from 16 to 24 or from 24 to 36 sec). He observed a decrease in the rate of responding with fixed compared to random ISIs, but there was no effect on the amplitude of the K-Complex. An interaction between the rate of presentation and the predictability of stimulus occurrence was also found. The probability of eliciting a K-Complex increased with decreases in the rate of presentation when a fixed ISI was used. No effect of the ISI was noted with the random ISIs. Campbell et al. (1985) used somewhat similar ISIs, being either 5, 10, 20 or 30 sec and of only fixed intervals. Like Firth (1973), they found that the longer the ISI, the more often a K-Complex could be elicited. The amplitude of the averaged K-Complex did not differ when the ISI was 10 sec or

longer although it was attenuated when a 5 sec ISI was used. Again, averaging was carried out whether a K-Complex was elicited or not. The averaging procedure could therefore have led to a false conclusion. The average of all trials in a condition was a poor reflection of individual, single trial K-Complexes.

McDonald, Schicht, Frazier, Shallenberger and Edwards (1975) studied the effects of long ISIs that varied from 20 to 60 sec. No increase in the probability of eliciting a K-Complex was observed with longer ISIs. Similarly, Jonnson et al. (1975) did not observe any effect of an ISI that varied from 30 to 60 sec. Ujszászi and Halász (1986, 1988) presented stimuli at ISIs varying between 15 and 120 sec. They also did not report any significant differences in the rate of responding or in the amplitude of the single trial K-Complex.

In spite of what appears to be a rather disparate literature, a consensus may be possible. Increasing the ISI beyond 10 to 15 sec has been consistently shown to have little chance of increasing the number of K-Complexes. When the ISI is less than 10 sec, an effect on the number of elicited K-Complexes has generally been found.

Tonal Frequency

Most laboratories employ a tonal frequency between 500 and 2000 Hz. There has been little attempt to systematically determine its effect. However, Campbell et al. (1985) did report that K-Complexes occurred more often with higher (2000 Hz)

than with lower (500 Hz) frequencies. No explanation of this phenomenon was reported.

Duration

The duration of the auditory stimuli used in the different studies when reported has varied from 10 msec to 90 sec. Most studies did not systematically manipulate this parameter but Campbell et al. (1985) did study its effect. They reported that the amplitude of the K-Complex was attenuated with short (10 msec) and long (1 sec and 5 sec) durations compared to a 100 msec duration tone. Again, this could be an artifact of their averaging procedure, since K-Complexes occurred more often to the 100 msec duration tone than to those having either very short or very long durations. Interestingly, when a K-Complex was elicited, it occurred to stimulus onset rather than its offset (Campbell, personal communication).

Rise-and-Fall time

The rise-and-fall (R/F) of the auditory stimuli used in the different studies varied between 1 and 40 msec. Again, most previous studies did not systematically manipulate this variable. Campbell et al. (1985) reported that the N550 component was larger with fast (1 and 10 msec) than with slow (20 and 40 msec) rise-and-fall times. They therefore suggested that the K-Complex may be a Defensive Response ("DR") since they are most often

elicited by abrupt (i.e., having fast rise-and-fall times), loud stimuli.

Psychological significance

Oswald et al. (1960) presented taped names to their subjects (subject's own name and other different names) and found that K-Complexes were elicited more often when the subject's own name was presented than when it was a different name or when the name was played backwards. Frazier, McDonald and Edwards (1968) also presented taped names and compared these K-Complexes to K-Complexes elicited by tones. Their results also showed a greater number of K-Complexes when the subject's own name was presented, but the probability of occurrence did not differ when tones and names other than the subject's were used as stimuli.

Probability of occurrence of the stimulus

Salisbury, Squires, Ibel and Maloney (1992) measured a series of auditory averaged evoked potentials that they labelled "N2-P3-N3" during an oddball task ("standard" and "deviant" stimuli are presented, the standard stimulus having a much higher probability of occurrence than the deviant stimulus). In a first condition (loud, rare condition), a "standard" 40 dB HL, 250 Hz "soft" stimulus was presented every 1.2 sec. On 10 % of the trials, the standard was randomly changed to a "deviant" 60 dB HL, 3000 Hz "loud" stimulus. In a second condition (soft, rare condition), the standard loud stimulus was 60 dB HL 3000 Hz while

the deviant soft (40 dB HL, 250 Hz) stimulus was again presented on 10 % of the trials. N2 was identified as a negative wave peaking at about 200 msec, P3 a positive wave peaking at approximately 300 msec, and N3, a negative wave peaking between 450 msec and 800 msec. The authors noted that the amplitudes of N2 and P3 were larger when subjects were awake than when they were sleeping. N3 was, however, larger in sleep, and was also larger following deviant than standard stimuli. They suggested that N3 probably was affected by K-Complex activity. High amplitude may have been elicited by the rare, deviant stimulus. Trials that were averaged were not sorted according to those in which a K-Complex was elicited and those in which it was not. Highly deviant stimuli probably elicited more K-Complexes. If so, on average, N3 (or N350) would appear to be larger than on trials on which a K-Complex was not elicited because the massive N550 might "pull up" (assuming negative polarity is "up") the much smaller N3. Again, the average of all trials (whether they elicit a K-Complex or not) will not be a true reflection of a single trial K-Complex.

Measurement of the K-Complex

Several factors have been reported to affect the amplitude of the K-Complex, including age, stage of sleep and stimulus parameters. Many methodologic discrepancies for the definition and measurement of the K-Complex are, however, apparent. The K-Complex occurs in NREM sleep, a period in which high amplitude

slow waves often dominate the background EEG. As mentioned, high amplitude slow waves may mask the K-Complex. Indeed, during stage 4 the K-Complex may be impossible to detect. Even when it is visible (in stage 2), it will "ride" on top of the background EEG. This background "noise" will summate with the K-Complex. The amplitude of single K-Complexes will thus show considerable trial-to-trial variability due to this overlapping background noise. Differences in many of the early studies may have been due to the fact that they were limited to measuring single, isolated K-Complexes. The differences could thus be due to random background noise.

As mentioned, in some recent studies averaging techniques have been used to reduce the background noise of the EEG. Averaging techniques require that the "signal" be time-locked to a particular event. In the case of the evoked K-Complex, this is the stimulus. Since stimuli are repeatedly presented and the amplitude of the background noise is random, over an infinite number of trials, the summation of random activity should tend toward zero. Thus the random noise should cancel itself with the averaging process. The amplitude of the signal is constant. The average of a constant is that constant. With repetition of the stimulus, the evoked K-Complex will begin to become clearer as the background noise becomes attenuated. Averaging cannot be employed with the spontaneous K-Complex since there is no single event or feature that can be used to synchronize (or "time-lock") the average.

When K-Complexes have been time-locked to external stimuli and averaged, the technique has been used indiscriminantly. The theory of signal averaging assumes that the signal is constant in time and amplitude (it occurs at the same time and its amplitude does not vary). On certain trials, a K-Complex will be elicited by a stimulus and on certain trials (for whatever reason), it will not. It is inappropriate to average trials on which a K-Complex is elicited with those on which it is not. In such cases, the "average" K-Complex will be a poor reflection of single trial K-Complexes.

The measurement of the K-Complex differs from study-to-study. Many laboratories measure the K-Complex from the highest peak deflection of the large negative wave (N550) to the valley of the following large positive peak (P900). Peak-to-peak measurement assumes that both peaks have a similar function (i.e., they are not functionally independent) and have identical intra-cranial generators. This may not be the case. Variation in the amplitude of one peak, independently of the other, will not be detected by peak-to-peak measurement. An alternative measure employs a baseline-to-peak measure. A baseline is drawn (usually the average of activity prior to stimulus presentation) from which peaks are measured. Baseline-to-peak measurement is sensitive to the functional independence of each of the different peaks.

Often, single electrode placements are employed. The K-Complex appears to consist of a series of different components,

rather than a single entity. The independence of different components can be established by either experimental manipulations or different scalp topographies. The scalp topography of the K-Complex can only be determined from multi-channel recordings.

K-Complexes have been recorded at different times of the night and in different stages of sleep. Halász et al. (1985) observed that the amplitude of the K-Complex varied as a function of depth of sleep. A number of other studies (Weitzman and Kremen, 1964; Church et al., 1978; Rajna, Halász, Kundra and Pál, 1983) have previously agreed that the K-Complex was larger in stage 3 and 4 than in stage 2 although it occurred less frequently. Still other studies insist that the K-Complex cannot be detected at all in Stage 3 and 4. As mentioned, this is because it is buried in the background noise of the high amplitude delta waves. When averaging techniques are used, a K-Complex can clearly be seen in stage 4 (Campbell et al., 1985). Previous studies have reported that K-Complexes were more easily elicited at the beginning than at the end of the night (Halasz et al., 1985). Others did not find these differences (Paiva and Rosa, 1991). Nevertheless, since stage 2 appears in both the beginning and the end of the night, it is possible to control for possible time-of-night effects.

Consequences

Statements about the antecedents of the K-Complex do not constitute a theory but help understand how and in which conditions it will most likely be elicited or will occur. As mentioned earlier, stimulus parameters and the stage of sleep are important antecedents for the occurrence of a K-Complex. These antecedents do not, however, explicitly point to the functional role or significance of the K-Complex. Donchin and Coles (1988), while studying the P300 component of the evoked potential, claimed that the ultimate goal of a "psychophysiological" theory is to elucidate the nature of the task, the occurrence of a phenomenon. By "functional significance", Donchin and Coles (1988) implied that "the potentials recorded at the scalp are manifestations of the intracranial activity of a specific functional entity". As such, even if the K-Complex is affected by different stimuli and not others, if it occurs in NREM sleep and not in REM, no explanations can be given regarding its functional role in sleep. Furthermore, even if the intracranial generators are known, this would offer little in the way of understanding the function of the K-Complex.

Arousal reaction

The function or role of the K-Complex remains an area of much debate. Loomis et al. (1939) thought that the K-Complex was a forerunner of delta waves since they believed the K-Complex mainly appeared before deep sleep (stage 3 and 4). Davis et al.

(1939) later distinguished early from late components and interpreted the early component as a reflection of arousal caused by stimulus presentation (either internal or external). They observed that the earlier waves were not readily apparent in K-Complexes that occurred during Stage 3 or 4 of sleep. This was proposed to be due to the inability to arouse the subject from deep sleep. Such a line of reasoning is of course quite circular. Davis et al. (1939) speculated that the late component was a delayed generalized response of the cortex to sensory stimulation. They had little evidence to support this claim. Gibbs and Gibbs (1950) considered the K-Complex as a state similar to wakefulness. Bancaud, Bloch and Paillard (1953) agreed with Gibbs and Gibbs (1950). They noted a modification in the skin resistance simultaneously with the occurrence of a K-Complex. In both instances, the K-Complex was considered to serve an arousal/information processing role. Again, there was little systematic attempt to test this theory.

Roth et al. (1956), in an extensive study, compared spontaneous and evoked K-Complexes within the different stages of sleep. K-Complexes were elicited by many different stimuli that varied in modality (auditory, visual and tactile), intensity and under different conditions (drug, sleep loss and natural sleep). In spite of these stimuli and arousal differences, the amplitude of the single trial K-Complex (i.e., K-Complexes observed to occur to single stimuli) did not vary. They therefore claimed that the K-Complex was an "all-or-none phenomenon". The K-

Complex was either elicited or was not elicited by the stimulus. When it was elicited, its amplitude remained constant in spite of manipulation of the physical stimulus. Its function was hypothesized to be a correlate of a "crude perceptual process which tended to initiate arousal".

In contrast, Oswald et al. (1960) observed that the psychological significance of the stimulus (as opposed to its physical quality) did affect the amplitude of the K-Complex. Subjects heard a list of names, some of which were played backwards. The K-Complex occurred most often and was largest in amplitude when subjects heard their own name and occurred least often when the names were played backwards (and hence were not significant). They thus concluded that the K-Complex reflected the content of information processing during sleep. In this regard, Oswald et al. (1960) considered the K-Complex to be an Orienting Response (OR).

Johnson and Karpan (1968) recorded heart rate (HR) concurrently with the EEG. They observed an acceleration of the HR following the occurrence of a spontaneous K-Complex. During wakefulness, a number of studies have now reported that the HR decelerates following stimuli that elicit ORs (Jackson, 1974; Putnam, 1990; Graham and Hackley, 1991). The pattern of HR changes following a K-Complex (i.e., acceleration) is therefore incongruent with what would be expected following an OR (i.e., deceleration). Loud and abrupt or painful stimuli cause HR acceleration. This is called a Defensive Response (DR). From

this perspective, the K-Complex therefore seems to be more compatible with a DR than an OR. Muzet (personal communication with K. Campbell) has also indicated that vasoconstriction is observed following a K-Complex. Vasoconstriction is also a component of a DR.

A means to resolve the question of whether the K-Complex is an OR or a DR is to determine if it is subject to habituation. The magnitude of the OR is reduced upon repetition of the stimulus. This reduction in the OR with repetition is the habituation process (McDonald and Carpenter, 1975). Unlike ORs, the DRs are not subject to habituation. Responses that are said to have habituated are marked by a gradual decline in amplitude followed eventually by a complete failure to respond (Thompson and Spencer, 1966). Studies examining habituation of the K-Complex have produced equivocal results. Johnson and Lubin (1966) did not observe habituation while Firth (1973) and MacDonald et al. (1975) did. These latter authors did not define "habituation" according to Thompson and Spencer's criteria. Habituation was claimed to occur when the *rate* of responding decreased when the ISI was shortened. Rate of responding is, of course, not equivalent to a diminution in the amplitude of the response. More recently, Caekebeke, van Dijk and van Sweden (1990) observed a decrease in the amplitude of the negative (N550) wave following repetition of the stimulus. They interpreted the decrease in amplitude as a reflection of an habituation processes. Moreover, when a novel stimulus was

presented following a train of repetitive stimuli, they observed "dishabituation" (a return to full amplitude of the N550 wave). Caekebeke et al. (1990) employed averaging techniques to reduce the contribution of background noise. Normal averaging procedures cannot be used to examine trial-to-trial variation in the K-Complex.

A reason that would explain why such discrepancies exist between studies might be that the measurement of the K-Complex varied from one study to the other. The definition of what is considered to be a K-Complex, as mentioned earlier, varies from laboratory to laboratory. Some studies looked at single trials (Firth, 1973) while others (Caekebeke et al., 1990) looked at averaged trials K-Complexes. Moreover, habituation has not been defined in the same way among the different studies (decrease in the amplitude of the response in some studies or decrease in the rate of responding in others). Previous studies cannot therefore resolve the OR-DR and habituation dilemma.

Protection of sleep

Walter (1963) claimed that "the appearance of a K-Complex is a sign the sleep is deep and hard to disturb, and it seems to act so as to muffle the arousal stimulus". He metaphorically suggested that "like the dream that explains away the unwelcome alarm bell, K-Complexes seem to flatten the significance of intrusive signals, so that the sleeper's standard of meaning is stretched beyond the tolerance of waking life". Walter thus

implied that K-Complexes seemed to protect the sleeping brain from awakening by disguising the stimulus, it thus becoming insignificant to the subject. Hess (1965), like Walter, thought that K-Complexes reflected a process that protects the brain from unnecessary arousal reaction. Halász (1981), as mentioned, studied generalized epilepsy with spike-wave paroxysms. He showed similarities between the K-Complex and the spike-wave pattern. His studies led him to conclude that "the K-Complex was a rebound reaction on the part of the sleep promoting process arising in response to sensorial impulses transmitted through the reticular arousal system". Halász (1981) also considered the K-Complex as being a "building stone" to the process of falling asleep.

Two opposing theories have thus arisen to explain the role of the K-Complex. One maintains that the K-Complex is a response to a significant stimulus that provides a mechanism to arouse the subject from sleep. The opposing theory maintains that the K-Complex is also a response to a significant stimulus which is, however, not so significant that sleep should be disturbed. The K-Complex thus serves to drive the subject into deeper sleep. In spite of more than 50 years of research, there has been little systematic empirical testing of these opposing theories.

The subject of this thesis

Most studies have considered the K-Complex to be a functional unit (particularly the N550-P900 wave). It is now generally accepted that the K-Complex consists of a large negative-positive wave peaking at approximately 550 and 900 msec respectively. A third earlier negative wave, peaking at approximately 350 msec, is also considered by many to be part of the K-Complex. A few authors have attributed different functions to the different peaks. N550 was thought to be an index of arousal by Davis et al. (1939) while P900 was thought to be an index of attention and/or memory by Graham and Clifton (1966). Again, there are little data to support either claim. The role of N350 remains poorly understood.

Previous studies have reported that the probability of occurrence of the K-Complex varies in the different stages of sleep. More K-Complexes can be identified in stage 2 than in stages 3 and 4, but this could be due to the ease in detecting K-Complexes in the background EEG. A means to resolve this issue taken in this thesis will be to study the average of single evoked K-Complexes by using a standard set of algorithms for the identification of a single K-Complex. Stimulus-locked evoked K-Complexes are easily discernable in Stage 3 and 4 when appropriate averaging techniques are used. Trials will be sorted into those in which a K-Complex is elicited and into those in which the K-Complex is not elicited. This categorisation will assure that the averaged response will be a reflection of the

single trial K-Complexes. Finally, since Stage 2 appears at both the beginning and the end of the night, it will be possible to control for time-of-night effects by subdividing Stage 2 data according to early and late portions of the night.

Because of controversies in the literature, an initial study will determine the types of stimuli most likely to elicit the K-Complex. In particular, the effects of stimulus intensity, tonal frequency and rise-and-fall time will be assessed. This is required to distinguish whether the K-Complex is an OR or a DR. DRs are elicited by loud, abrupt stimuli. There is some question whether the amplitude of the K-Complex is independent of the physical qualities of the stimulus (i.e., is an all-or-none phenomenon). This is probably because most studies have attempted to measure single trial K-Complexes where the background noise may cause considerable trial-to-trial variation. Under these conditions, only very large and consistent trial-to-trial differences will be found to be statistically significant. The statistical power to actually reject the all-or-none hypothesis is thus limited. Signal averaging techniques will be used to reduce the background noise thus providing an excellent means to compare variation of the K-complex with different stimulus characteristics.

A second study will examine the influence of the rate of stimulus presentation on the evoked K-Complex. The rate of stimulus presentation has been a factor long-known to affect the likelihood of eliciting a K-Complex (Roth et al., 1956). It

would appear that as the rate of stimulus presentation is slowed (up to about 10 sec), the probability of eliciting a K-Complex increases. Beyond 10 sec however, there appears to be little change in the probability of eliciting a K-Complex. By contrast, little is known about how the rate of presentation affects the amplitude of the K-Complex. In the second experiment, averaging techniques will again be used to reduce background noise. Various rates of stimulus presentation will be employed.

The foregoing studies were designed to examine the antecedents of the K-Complex. The final study examines the consequences of the K-Complex. It will evaluate the functional role of the K-Complex by carrying out a spectral analysis of the EEG prior to and following the stimulus. A comparison of trials on which a K-Complex is elicited with trials on which it is not will be made to determine the effects of the stimulus itself on the EEG power spectra. The results of this study will be used to determine if the K-Complex is an index of arousal or is a sleep-protecting mechanism. High frequency and low amplitude waves (e.g., beta) are usually indicative of arousal while slow frequency and high amplitude waves (e.g., delta) are usually indicative of deeper sleep. If the K-Complex is an index of arousal, higher frequencies should show increased power after the occurrence of the evoked K-Complex. However, if the K-Complex is an index of a drive into deeper sleep, lower frequencies should show increased power following stimulus presentation.

Table 1

Authors	N	Stimuli	Electrodes	Stages	Components	Results
Loomis, Harvey and Hobart (1939)	10	tone stimulus	6 diff sites (??)	A,B,C,D and E[1]	disturbances patterns, spindles	- K-Complex can be spontaneous or evoked
Davis, Davis, Loomis, Harvey and Hobart (1939)	1	tone, 70 dB, 500 Hz, light, electric shocks	Fz, Cz and Oz	A,B,C,D and E	K-Complex (one negative and one positive component)	- ¶ K-Complex higher before Delta - K-Complex can be evoked by different stimuli
Roth, Shaw and Green (1956)	80 15	sound (speaker) visual painful shock tactile	Cz-Oz Fz-T5 T6-Oz T3-T4	wake, A, B, C, D	Fast and Slow wave Spindle	20% responses ISI>3 sec: continuous responding ISI<3 sec: intermittent responding ISI<1 sec: suppression - Not refractory: ISI>3 sec provided continuous responding without any observable decrease in the amplitude of the large and slow waves - all-or-none phenomenon - should always be followed by a spindle
Oswald, Taylor and Treisman (1960)		taped names, (speaker) ISI: 5, 7, 4, 8, 6 sec	Fz-Cz-Pz	C and D of Loomis et al. (1937)	Large Wave Slow Wave spindle (K, R, N classification)[1]	- ¶ K-complexes higher to own name - K-Complex is a discriminative response - K-Complex disappears in Delta sleep - No significant differences in probability, amplitude or latency with different ISIs
Weitzman and Kremen (1964)	10	auditory click (speaker) 50-60 dB above threshold, 0.5 msec duration	vertex right occ.	all stages of Dement and Kleitman(1957)[1]	P1 N1 P2 N2 P3	- N2-P3 amplitude is higher in deep sleep - K-Complex in NREM sleep only - K-Complex exists in Stage 4 - AER in sleep: summed K-Complexes - N2: 325 msec - P3: 850 msec
Johnson and Lubin (1966)	15 3N	30-35 dB above threshold, 1000 Hz 3 sec duration, ISI 30-45 sec	P3-P4, O1	wake, stage 2 of Dement and Kleitman (1957)	K-Complex (negative-positive complex, no μV criterion), HR, GSR, FFR, SPR, PR	- no habituation, rate of responding did not change throughout the night - when a K-Complex is elicited, all other responses are enhanced
Sassin and Johnson (1968)	5 2N	no stimulation	F3, C3 and P3	Stages 2, 3, 4 and REM	Spontaneous K-Complex (negative-positive complex, no μV criterion) HR, FFR	- Body movements were significantly related temporally to preceding K-Complexes in stage 2 sleep - HR acceleration following K-Complexes
Frazier, Mc Donald and Edwards (1968)	13 2N	taped names, tone, (speaker) 75 dB, 500 Hz, 500 msec duration, ISI<1 sec	Oz, Pz	All sleep stages de Rechtschaffen and Fales (1968)	K-Complex (negative-positive complex of high amplitude) GSR, HR, RR, FFR	- The K-complex is larger to own name than tone but not to other name - tone not different than other name

Firth (1973)	3 3N	tone (Speaker) 70 dB, 1000 Hz, 1 sec duration, Fixed ISIS: 10, 20, 30; Random ISIS: 8-10-12, 16-20-24, 24-30-36,	Fz, Fz-Pz	stages 2, 4 and REM	K-Complex (negative-positive complex with spindle) K, R, N classification of Oswald et al. 1960), Sw, HRR	- K-Complexes rate decreases with short and regular ISI, interpreted as evidence for habituation.
Mc Donald, Schicht, Frazier, Shallenberger and Edwards, (1975) exp 1	13	25 different taped names, tones (speaker) 75 dB, 500 Hz, 500 msec duration, ISI: 20 to 60 sec (X:40)	P3, P4Mw, O2	wake and all stages of Rechtschaffen and Kales (1968)	K-Complex (absent or present, negative-positive complex), FRR, HRR, SR, SP, RR	- K-Complex larger to own name - K-Complex larger to other name than sounds
Mc Donald et al. (1975) exp 2	24	horns (speaker) 40 dB, 200 or 2000 Hz, 1 sec, ISI: 30-90 sec (X: 45) CS+, CS- 110 dB, 500 msec duration	P3, P4 O1, O2	stages 2, 4 and REM	K-Complex (absent or present, negative-positive complex). FRR, HRR, SR, SP, RR	- Conditioned discrimination is maintained in stages 2 and 4
Johnson, Townsend and Wilson (1975)	46 5	1- tone pips, (speaker), 75 dB, 800 Hz, 1 or 2 sec duration, ISIS: 30, 45, 60 sec 2- tone pips, (speaker) 70 dB, 800 Hz, 1 sec duration ISI: 10 sec	C3, C4, O1, O2	stage 2 only	K-Complex (negative-positive complex), SR, SP, HR, FP	- No habituation of K-Complex (rate of responding does not change under different ISIS)
Johnson, Hanson and Bickford (1976)	5 14N	no stimulation drug: flurazepam	C3, C3-O1	stage 2 only	Spontaneous K-Complex (negative-positive complex) with or without Spindle, Spindle	- increase in the rate of spindle bursts, decrease in the number of K-Complexes
Church, Johnson and Seales (1978) exp 1	12	44 dB, 1000 Hz, 10 msec duration (speaker) - delivery lock to spindle	C3-C4	stage 2 only	K-Complex defined as N500-P1000, spontaneous and evoked, HR	- More K-Complexes when stimuli delivered at the time of a spindle than any other time - K-Complex larger with spindle- synchronous (SS) than spindle-asynchronous (SA)
Church et al., (1978) exp 2	7	same stimuli as for exp 1 ISI 30 sec	C3	stages 2, 3 and 4	K-Complex N500 and P1000	- K-Complex larger in SS than SA; larger in stage 3-4 than 2 - More K-Complexes in SS than SA

Takigawa, Uchida and Matsumoto (1980)	11	no stimulation	left and central gyrus	stage 2 only	Spontaneous K-Complex (negative-positive complex), HR, RR	- Within 3000 msec from the beginning of respiration cycles, spontaneous K-Complex occur more frequently in the former and middle part of inspiration, whereas in the whole period of expiration its occurrences tend to be distributed evenly - latencies of components inspiration: 200-300, 400-600 and 800-900 - latencies of components expiration 400-500, 800-900 and 200-300
Takigawa and Taira (1980)	10	clicks (speaker) 15 dB, ISI: 10 sec	left and central gyrus	stage 3 only	K-Complex (negative-positive complex) AEP: N1, N2, N3, N4	- K-Complex consists of 3 deflections. 1) sharp wave 2) slow wave 3) 12-14 c/sec 1 + 2 = s-components - Evoked K-Complexes (s-components) in the EEG were almost equivalent to the AEPs (N4-component) if both were concordantly recorded time-locked to click stimuli
Ehrhart, Ehrhart, Muret, Schieber and Naitoh (1981)	6	Airplane noise: (speaker) 1) 77 dB, 90 sec duration; 2) 80 dB, 30 sec duration; 3) 82 dB, 90 sec duration; 4) 96 dB, 30 sec duration; 4 noises/hour	P3-P3 Cz	stages 2 and 3	K-Complex (negative-positive complex) Spindles	- 4 different K-Complexes: 1) K0: no spindle 2) K1: spindle prior 3) K2: spindle during 4) K3: spindle after - Spindles have an inhibitory effect on the K-Complex - Spontaneous K-Complexes and sleep spindles act antagonistically: spontaneous K-Complex reflect anorganismic state leading towards the "phase d'activation transitoire" (PAT) while sleep spindles inhibit PAT - No effect of intensity was observed
Rajna, Halasz, Kundra and Pal (1983)	6	clicks (speaker) 2000 Hz, 10 msec duration, ISI: 20 sec; visual: whiteflash 0.045 MS	?	stages 2, 3 and 4	K-Complex negative and positive peaks between 450 and 1500 msec	- K-Complex amplitude increases on descending limbs of sleep cycles and decreases on ascending limbs - amplitude is positively correlated with the deepening of sleep (amplitude is largest in stage 4)
Campbell, Bell and Deacon-Elliott (1985)	10	tone pips (hearing-aid) 80 dB SPL, 2000 Hz, 100 msec duration, 10 msec R/F, ISI: 10 sec; a) intensity 80, 70, 60, 50; b) frequency 0.5, 1, 2, 4 kHz; c) duration 10, 100, 1000, 5000 msec; d) R/F: 1, 10, 20, 40 msec; e) ISI: 5, 10, 20, 30 sec	Fz Cz Pz	stages 2, 3, 4 and REM (stage 2 divided in 2a and 2i and stage 3-4 combined as SWS)	Averaged K-Complex N550-P900'	-N550 and P900 maximum at Fz - no amplitude differences throughout the different stages of sleep - significant amplitude decreases with decreases in intensity -frequency does not affect the morphology of the K-Complex -amplitude is larger to shorter than to longer durations -R/F: amplitude increases to 1 and 10 msec, amplitude decreases to 20 and 40 msec -amplitude not different for 10, 20 and 30 sec ISI. N550 amplitude is smaller for 5 than 10, 20 and 30 sec ISI
Pal, Simon and Halasz (1985)	3	tone pips (speaker) 1000 Hz, 20 msec duration, ISI: 10-16 sec	C3, C4	stage 2 only	K-Complex defined criteria, special set of algorithms	- Presence of evoked K-Complexes can be predicted from the power density function of 1.8 sec EEG epoch preceding the stimulus

Halasz, Pal and Rajna (1985) exp 1	8 5N	clicks (speaker) 200 Hz, 10 msec duration; ISI: twice every 40 sec, vis: whiteflash 0.045 MS	Cz-O1 Cz-O2 Cz-T3 Cz-T4	stages 2, 3 4 and REM	K-Complex defined criteria, special set of algorithm	- higher % of K-Complexes on ascending slopes than on descending slopes - frequency of K-Complexes decreases from evening to morning, from cycle to cycle
Halasz et al. (1985) exp 2	1 21- NS 14S	clicks (speaker) 60 dB, 1000 Hz, 10 msec duration; ISI: 2-20 sec, vis: whiteflash 0.045 MS	same as exp 1	stages 2, 3 4 and REM	same as exp 1	- More frequent K-Complexes and less spontaneous K-Complexes on stimulated than non-stimulated nights
Halasz et al. (1985) exp 3	1 6S	same as for exp 2 but 5 min of stimulation followed by 5 min of no stimulation	same as for exp 1 and exp 2	stages 2, 3 4 and REM	same as exp 2	- More frequent K-Complexes and less spontaneous K-Complexes in stimulated than non-stimulated periods
Ujszászi and Halász (1986)	6 2N	tone pips (speaker)60 dB, 1200 Hz, 70 msec duration, ISI: 15 to 120 sec	Cz	stage 2 only	K-Complex (negative-positive complex)	- 3 different K-Complex. N100-P400, N100-P800 and N600-P800
Ujszászi and Halász (1988)	10	tone pips (speaker) 70 dB, 1200 Hz, 70 msec duration, ISI: 20 to 120 sec	Fz, Cz, Pz	Stages 2, 3 and 4	N100 P200 N300 P400 N550 P900 N1500 P1900	- K-Complex consists of 3 different components: N100 (maximum at Cz), N550 (maximum at Fz), and P900 (maximum at Pz)
Caekebeke, van Dijk and van Sweden (1990)	6	tones pips (speaker) 1-0 dB dummy, 5-65 dB, 2000 Hz and 5-65 dB, 3000 Hz; 50 msec duration, ISI: 5 sec,	?	Stages 2, 3 and 4	Averaged K-Complex (negative-positive complex) Spindle	- K-Complex (the delta wave) habituates to 2000 Hz and 3000 Hz stimuli and dishabituates to the first 3000 Hz stimulus following the 2000 Hz stimuli. Habituation is defined as a decrease in the amplitude of the delta wave component of the K-Complex.
Caekebeke, van Dijk, Rosa and Kemp (1991)	8	tones (loudspeaker) 14-2000 Hz 86-1000 Hz, 50 msec duration ISI: 1.5 sec	Fz, Cz, Pz	Stages 0-1, 2, 3-4 and REM	K-Complex, averaged P70 (P1); N120 (N1); P200 (P2); N400 (N4); P < 750 msec (P3)	- Higher amplitude after infrequent stimuli - early components present with little variability in all sleep stages - infrequent stimuli = P2-N2-P3 complex in stages 2 and 3-4 which hardly exists after frequent stimuli - difference between frequent and infrequent stimuli probably reflects habituation to frequent stimuli - late complex of K-Complex could be described as arousal reaction
Halász and Ujszászi (1991) exp 1	5	tone pips (loudspeaker) 70 dB, 1200 Hz, 50 msec duration, R/F 20 msec, ISI: 30 sec (with 25% random variation)	Fz, Cz, Pz	2, 3 and 4	MAs (K-Complex, spindle)	- strong increase in power followed by a gradual reduction after stimulus - 13-14 Hz spindle range: little variations in this range for first 2 seconds post-stimulus but strong and sustained depression at 3 seconds with no recovery within 10 sec post-stimulus

Halász and Ujszászi (1991) exp 2	4	tone pips (loudspeaker) 83 dB, 1300 Hz, 10 msec duration, ISI: 35 sec (with 25% random variation)	Fpz, Fz, Cz, Pz, Oz	2, 3 and 4	no response (*NR*); K-Complex < 2 sec (*K*); K-Complex with sigma spindle (*KS*); K-Complex with alpha spindle (*KA*); polyphasic K-Complex or with delta (*KD*)	- *NR*: small peak after first post-stimulus second; no recovery within 15 sec - *K*: elevation lasting 2 sec in the power of delta and alpha with recovery within 15 sec; in 14 Hz frequency pronounced depression remained - *KS*: strong depression in sigma band; recovery for alpha and delta by 6 sec - *KA*: power elevation in alpha for 5 sec; following slight reduction in alpha band but not in delta and sigma - *KD*: similar to *KA*; both alpha and delta showed a long-lasting power elevation in the first half of the response without any significant depression in the consecutive epochs - post-stimulus spectral pattern is characterized by a short initial power elevation and a following reduction in delta, theta, alpha and beta frequency and a strong power reduction at 13-14 Hz sigma spindle band
Paiva and Rosa (1991)	5	no stimuli	F4, Fz, F3 C4, Cz, C3 O2, Oz, O1	1, 2, 3 and 4	spontaneous K-Complex (6 types); with spindle or other phenomena (phasic activity)	- Higher % of *K*-Complexes in frontal regions - Higher % of biphasic *K*-Complex, *K*-Complex with spindle after - Higher % of isolated *K*-Complex than with vertex or delta waves - High inter-subject variability

Sleep stages as classified by Loomis and al.(1937):
A: interrupted alpha: the normal waking 10-per-second rhythm dominates the pattern
B: low voltage: the alpha rhythm is lost
C: spindles: short groups ("spindles") of 14-per-second waves appear and also random "delta" waves 0.2 second or more in length
D: spindles plus random: both types of wave increase in voltage and the delta waves become longer
E: random: the 14-per-second waves become inconspicuous, but delta waves continue to increase in voltage and wavelength

K-Complex classification of Oswald et al. (1960):
K: evident K-Complex (both negative and positive components);
R: K-Complex with only one component;
N: absence of K-Complex

Sleep stages classification of Dement and Kleitman (1957) after the observation of the presence of REM sleep in the ongoing sleep EEG.

Single trials to tone pips were stored on-line and then averaged together according to time of night and the different conditions.

Chapter 2

Experiment 1

The Evoked K-Complex: All-or-None Phenomenon?

Introduction

More than 50 years ago, Loomis, Harvey and Hobart (1939) noted that the presentation of an external auditory stimulus to the sleeping subject could elicit a very large amplitude waveform, the K-Complex. In the same year, Davis, Davis, Loomis, Harvey and Hobart (1939) observed that this waveform could also occur spontaneously without any apparent external stimulation. It is now known that K-Complexes appear in stages 2, 3 and 4 of sleep (Roth, Shaw and Green, 1956; Halász, Pál and Rajna, 1985). They do not occur spontaneously and cannot be evoked in REM sleep or while the subject is awake.

The morphology of the K-Complex consists of a well-delineated negative wave peaking at approximately 550 ms (N550) followed by a positive wave peaking at approximately 900 ms (P900). An earlier negative component peaking at about 350 ms (N350) has also been considered to be part of the K-Complex by some authors (Ujszászi and Halász, 1986). The N350, N550 and P900 peaks have different scalp topographies. N550 and P900 are frontally and fronto-centrally distributed respectively while N350 is more evenly distributed over mid-lines areas of the scalp (Ujszászi and Halász, 1986).

A number of studies have now examined the types of stimuli that can elicit a K-Complex. The intensity of the evoking stimulus plays a critical role, the probability of eliciting a K-Complex varying directly with the intensity of the stimulus (Halász, Pál and Rajna, 1985; Church, Johnson and Seales, 1978; Campbell, Bell and Deacon-Elliott, 1985). Campbell et al. (1985) have also noted that tone pips having fast rise-and-fall times are more likely to evoke a K-Complex than those having slow rise-and-fall times. Tonal frequency and stimulus duration have no significant effect (Campbell et al., 1985; McDonald, Schicht, Frazier, Shallenberger and Edwards, 1975).

There has been considerable debate about possible amplitude variations of the K-Complex as a function of stimulus parameters. In a classic article, Roth et al. (1956) claimed that the K-Complex was an all-or-none response. The usage of this term was probably adopted from the "all-or-none" law describing the action potential of a neuron. Roth et al. (1956) claimed that the single trial K-Complex was an all-or-none response since manipulation of a wide range of stimulus parameters apparently did not alter its amplitude. On any trial, any stimulus might elicit a K-Complex and when it did, its amplitude did not vary.

Later research was more equivocal. For example, while Johnson and Karpan (1968) also observed that a stimulus will not elicit a K-Complex on every trial. However, when it is elicited, its amplitude does not vary in spite of manipulation of the physical qualities of the stimulus. On the other hand, Oswald,

Taylor and Treisman (1960) presented much more complex stimuli -- spoken names. Contrary to what would be expected of an all-or-none phenomenon, they found that the amplitude of the K-Complex increased in amplitude the more the spoken name resembled the subject's own name.

A number of methodological differences and limitations could account for the discrepancies among the various studies. There has been little consistency across studies with respect to the types of stimuli (clicks, tones, spoken words) used to elicit the K-Complex or the method of transducing the auditory signal (loudspeakers, earphone inserts). Furthermore, sample sizes tend to be small, thus limiting the statistical power to find differences. Another major problem is that the amplitude of the ongoing EEG is very large in the sleeping subject, particularly during slow wave sleep. This ongoing, random EEG will overlap and sum with the K-Complex. A good portion of the variation in the amplitude of the K-Complex will thus be due to the random, overlapping background EEG. It is thus highly unlikely that single trial K-Complexes can be reliably measured against the background EEG.

To overcome this problem, authors have relied on signal averaging techniques to reduce the background "noise". The evoking stimulus is presented repeatedly. The average of the random, background activity should tend to cancel out. The constant response, the K-Complex, will remain. Campbell et al. (1985) used such an averaging technique to determine the effects

of different stimulus parameters on the K-Complex. As mentioned, they observed that the probability of evoking a K-Complex increased as stimulus intensity increased, or as the rise-time of the tone pip became shorter. The amplitude of the "averaged" K-Complex was also dependent on the physical qualities of the evoking stimulus, contrary to the all-or-none principle. Its amplitude decreased as the intensity of the evoking stimulus decreased. Further, the amplitude of the K-Complex was dependent on the rise-and-fall time of the stimulus. Its amplitude was higher with fast rise-times and smaller with slow rise-times. There is however a confound in this study. Single trials were averaged regardless of whether or not they elicited a K-Complex. The apparently "averaged" K-Complex will be higher in amplitude when a train of stimuli elicit many K-Complexes than when few are elicited. It is thus quite possible that the amplitude of single K-Complex is consistent with the all-or-none principle even though the average is not. Clearly, the indiscriminate use of averaging techniques is inappropriate in these circumstances.

Finally, many studies measure the K-Complex from the peak of the large N550 wave to the peak of the large P900 wave. Such peak-to-peak measurement assumes a common functional significance of both peaks. This need not be the case. Furthermore, N550 and P900 waves have different scalp distributions. Peak deflections having different scalp distributions must have different intra-cranial generators (Näätänen and Picton, 1987). A baseline-to-peak measurement technique permits separate measurement of each

peak deflection and thus does not make the assumption that the two peaks are generated by identical cerebral processes.

The present study was designed to overcome many of these methodological limitations. The physical qualities of the evoking stimulus was manipulated in different stages of sleep. Trials were sorted according to those on which a K-Complex could and could not be identified in the background noise following stimulus presentation. Signal averaging techniques were employed to reduce background EEG activity that overlaps the K-Complex. To determine if the K-Complex is morphologically invariant in the different stages of sleep, single trials on which a K-Complex was evoked were averaged and compared in the different conditions. Similarly, trials on which a K-Complex could not be elicited, were also averaged. The effects of the manipulation of the physical qualities of the stimulus on the amplitude and latency of the N350, N550 and P900 deflections were then determined.

Methods

Subjects

Nineteen young adults (5 males, 14 females) between the ages of 20 and 35 ($\bar{X}$ = 24) participated in these studies. They were tested in a single all-night session. They were instructed to refrain from alcohol and drug use for 24 hours prior to the experiment. All subjects were asked to read and sign a consent form that provided details of the experimental paradigm and

procedures. Each subject received an honorarium for participating in the study.

EEG Recording

The EEG was recorded with Grass gold cup electrodes placed at midline frontal, central and parietal sites (Fz, Cz, and Pz) referenced to the left mastoid. The EOG was recorded with electrodes fixed at the supra-orbital ridge of one eye and the infra-orbital ridge of the other. This permitted the recording of horizontal and vertical eye movements on a single polygraphic channel. Inter-electrode impedance was maintained below 5 kOhms.

A pilot study was conducted to determine appropriate filter settings for the recording of the K-Complex. Four subjects were tested during stage 2 sleep. In these subjects, EEG was limited to a single Fz channel where the K-Complex tends to be at its maximum amplitude. This recording was fed into 8 different polygraphic channels. In five of these, the high filter was held constant at 15 Hz but the time constant was varied, being either 5.0, 2.0, 1.0, 0.3 or 0.1 s. In the other three channels, the time constant was held constant at 1 s and the high filters settings were varied being either 35, 70 or 500 Hz. Single K-Complexes were evoked by an 80 dB SPL tone pip. Trials were sorted according to those on which a K-Complex was either identified or not identified in the background noise. Those single trials on which a K-Complex was elicited were then averaged for each subject to reduce background EEG noise. A

minimum of 10 K-Complexes was used for the calculation of the average.

As illustrated in Figure 1, the filter settings had a marked effect on the K-Complex. The amplitudes of N550, P900 and the subsequent slow wave (between 1000 and 1500 ms) were attenuated by shorter time constants. Increasing the time constant beyond 1 s had minimal effect on the morphology of the K-Complex. A small amount of high frequency, background noise was visible with filter settings above 35 Hz. A time constant of 1 s and a high frequency filter of 35 Hz were therefore selected as a reasonable compromise for the recording of the K-Complex.

---------- Insert Figure 1 here ----------

Procedure

Each subject was individually fitted with a hearing-aid device through which the auditory stimuli were presented. The hearing-aid system assured constancy of stimulus input in spite of changes in the subject's head position during the night (Campbell and Bartoli, 1986).

Experiment 1

In Experiment 1, the intensity of the eliciting stimulus and its rise-and-fall time were manipulated. Seven subjects participated in this experiment. In the "standard" High intensity, Fast rise-time condition, nine consecutive 80 dB SPL 2000 Hz tone pips having a rise-and-fall time of 2 ms were

presented monaurally to the right ear of the subject. The inter-stimulus interval was 10 s. In the Low intensity condition, the intensity of the tone pips was lowered to 60 dB SPL. All other stimulus parameters were however held constant. In the Slow rise-time condition, the rise-and-fall time was increased to 20 ms with stimulus intensity held constant at 80 dB. The duration was increased to 70 ms to control for the amount of energy elicited by the short and long rise-and-fall time stimuli (Putnam, 1990).

Experiment 2

In Experiment 2, the frequency of the eliciting tone stimulus was manipulated. Twelve subjects participated in this study, none of whom had participated in the first experiment. Stimulus transduction and electrode placement were identical to Experiment 1. Twenty consecutive 80 dB SPL, 52 ms tone pips having a rise-and-fall time of 2 ms were presented monaurally to the right ear of the subject. The inter-stimulus interval was 10 s. The frequency of the stimulus was either 500, 1000 or 2000 Hz in different conditions.

In both experiments stimulus presentation began 15 minutes after the beginning of sleep onset (defined as the appearance of stage 2 or SWS). Each condition was presented in the different stages of sleep and repeated at least one more time to ensure replicability of the results. For most subjects, time permitted three repetitions of each of the different conditions.

EEG Analysis

The different stages of sleep were classified on-line by an experienced rater according to standard scoring criteria (Rechtschaffen and Kales, 1968). Testing occurred during definite stage 2, 3, and 4 of sleep. Stage 2 was subdivided into early (2E) and late (2L) halves to examine possible time-of-nights effects. Stages 3 and 4 were combined to form slow wave sleep (SWS). In the rare cases of stage classification ambiguity (less than 5% of conditions), records were later scored by a second, experienced rater. If the raters disagreed, the condition was rejected from further analysis. Stimulus presentation was discontinued and the trial rejected when the EEG sleep pattern showed signs of a stage change or upon subject movement.

EEG analysis began 300 ms prior to stimulus onset and continued for 1800 ms (i.e., 1500 ms post-stimulus). A total of 300 data points were digitized for each channel (i.e., the sampling rate was every 6 ms). The average of the pre-stimulus activity served as baseline from which peak deflections were measured.

Single trials were stored on-line and subsequently plotted. They were sorted into those trials identified as containing and not containing a K-Complex (in this case, a large amplitude N550-P900 wave). A set of algorithms was employed for the definition of a K-Complex. The trial had to have a negative peak between 400 and 650 ms ("N550") followed by a positive peak between 700

and 1200 ms ("P900"). Their peak-to-peak amplitude had to exceed 75 μV. Furthermore, the negative peak had to have a fronto-central maximum distribution. This algorithm was implemented to reject possible inclusion of random background noise as a K-Complex. This was especially necessary in SWS sleep during which isolated delta waves might be mistakenly identified as K-Complexes. An automatic computer scoring routine was used for the purposes of pattern recognition following these criteria (Bell, Campbell, Deacon-Elliott and Noldy-Cullum, 1988).

Single trials were sorted by condition, stage of sleep and whether they contained a K-Complex or not. They were then averaged to reduce random background noise.

Data Analyses

N350 was defined as the maximum negative peak in the 300-450 ms range, N550 as the maximum negative peak in the 450-700 ms range and P900 as the maximum positive peak in the 700-1200 ms range. To determine the effects of stimulus intensity a 4-way Anova was run having repeated measures on Intensity (High, Low), scalp site (Fz, Cz, Pz), stage of sleep (2 early, SWS, 2 late) and appearance of the K-Complex (Present, Absent). Similar 4-way repeated measures ANOVAs were run for the comparison of the effects of stimulus rise-and-fall time (Fast, Slow) and the effects of tonal frequency (High, Medium and Low). The analyses were carried out using the SAS PROC GLM procedure. Wilk's Lambda was employed to test for sphericity. Greenhouse-Geisser

corrections were employed when appropriate. Significant differences in probability of occurrence of K-Complexes across conditions were determined using multiple one-tailed t-tests. One-tailed directional t-tests were used since a priori expectations could be established on the basis of previous literature For all comparisons, the significance level was set at $p < .05$.

Results

Experiment 1

Across all conditions and stages of sleep, a K-Complex was elicited on approximately one-third of trials. The probability of occurrence in the Standard Condition was 0.50 compared to 0.20 for the Low Intensity. The probability of occurrence of a K-Complex for the Slow Rise-and-Fall time condition was 0.30. No significant differences were observed among the different conditions. K-Complexes were more likely to occur in stages 2E and SWS (0.42 and 0.35 probability respectively) than in stage 2L (0.23) but the differences were again not significant.

As mentioned, trials were sorted into those on which a K-Complex was identified and those on which it could not be identified. They were then averaged by electrode site, condition and stage of sleep. Figure 2 presents single trial data (randomly selected) for one subject (DC) and the average of these trials for the Standard condition. As may be observed, although there is some variability due to the overlapping large amount of

background noise, the average is a good reflection of the single trials. Although the large negative-positive complex is visible on most single trials, an earlier negative wave peaking between 300 and 400 ms could be discerned following averaging. As can also be observed, this earlier negative peak remains visible on the average of trials on which no K-Complexes could be identified.

---------- Insert Figure 2 here ----------

For the Standard condition, no significant differences were found for the probability of occurrence of K-Complexes among the nine consecutive trials within a block. From the first to the ninth trials, K-Complexes were identified on 61, 48, 48, 33, 61, 48, 61, 38 and 52% of the trials, respectively. When only trials containing a K-Complex were averaged, no significant differences were observed at Fz for either the amplitude or the latency of N550 and P900 among the nine trial positions. K-Complexes for each of the nine trials for the Standard condition are illustrated in Figure 3.

---------- Insert Figure 3 here ----------

Across both conditions and all stages of sleep, when a K-Complex was elicited, it consisted of a biphasic negative complex having peaks at 365 and 565 ms ("N350" and "N550", respectively)

and followed by a later positive wave, peaking at 935 ms ("P900"). N350 could only be discerned following averaging. It was embedded in the background EEG on single trials. For trials not containing the large N550-P900 complex, the N350 deflection still remained apparent. Different scalp topographies were observed for the different deflections. N350 tended to be uniformly distributed over mid-line areas of the scalp . It was maximum at Cz declining in amplitude by 16% at Fz and 33% at Pz . These differences did not reach significance. N550 was markedly frontally distributed declining in amplitude by 41% and 61% at Cz and Pz respectively ($F = 79.06$, $p < 0.01$). P900 had a more fronto-central distribution. It tended to be maximum at Fz, declining in amplitude by 21% and 33% at Cz and Pz respectively. However, these differences were not significant. The amplitudes of the different components (N350, N550 and P900) at each electrode placement are shown in Table 1 for the Standard condition.

---------- Insert Table 1 here ----------

The effects of stimulus intensity are illustrated in Figure 4. Amplitudes of the different components for the two intensities (60 and 80 dB) are presented in Table 2.

---------- Insert Table 2 here ----------

When a K-Complex was observed (again defined on the basis of N550-P900; left hand portion of the figure), N350 varied in amplitude from 14 to 45 μV in individual subjects or across conditions ($\bar{X}$ = 35.1, SD = 16.3 μV). In these trials, amplitude was not significantly affected by intensity (60 or 80 dB) or rise-and-fall time (2 or 20 ms) of the stimulus ($F < 1$ in both cases). Sleep stage had no main or interacting effects. Its amplitude was reduced by approximately 50% of trials on which no K-Complex could be identified. Moreover, on these trials, a decrease in stimulus intensity resulted in a significant attenuation (by, on average, 26%) of N350 amplitude ($F = 3.20$, $p < 0.02$). Manipulation of the rise-and-fall time had no significant effect on N350 amplitude. Stage of sleep had no main or interacting effects. No latency shifts were observed for any of the conditions or in any stage of sleep.

When a K-Complex was elicited, N550 amplitude varied from 45 to 164 μV ($\bar{X}$ = 77.5, SD = 26.6 μV) at Fz. No significant differences were found for amplitude ($F < 1$) or latency ($F < 1$) for either the manipulation of stimulus intensity or its rise-and-fall time. The K-Complex tended to peak earlier and was larger in SWS compared to 2 early and 2 late, although the differences were not significant ($p > .05$). When no K-Complex could be identified, N550 was not visible.

When a K-Complex was elicited, P900 amplitude varied from 15.5 to 74 μV ($\bar{X}$ = 47.5 μV, SD = 29.5). The P900 component followed the same pattern as the N550 on trials on which a K-

Complex could be identified. Thus, neither the manipulation of the intensity of the stimulus nor its rise-and-fall time significantly affected the K-Complex's amplitude or latency ($F < 1$ in both cases). On the other hand, in single trials in which a K-Complex could not be identified, only a very small amplitude P900 was visible in the averaged waveform.

---------- Insert Figure 4 ----------

Experiment 2

Across all conditions and stages of sleep, a K-Complex was elicited on approximately half of all trials (.50). The probability of occurrence in the 2000 Hz condition was 0.53 compared to 0.50 and 0.49 for the 1000 and 500 Hz conditions, respectively. No significant differences were observed among the different conditions. K-Complexes were more likely to occur in stages 2E and 2L (0.51 and 0.56, probability respectively) than in stage SWS (0.45), but again the differences were not significant.

The averaging procedure of Experiment 2 was identical to that used in Experiment 1. Thus, trials were sorted into those on which a K-Complex was identified and those on which it couldnot be identified. They were then averaged by condition and stage of sleep.

Across all conditions and sleep stages, when a K-Complex was elicited, it consisted of a biphasic negative complex having

peaks at 387 and 615 ms ("N350" and "N550", respectively) which was followed by a positive wave, peaking at 954 ms ("P900"). Again, N350 could only be discerned following averaging. For trials not containing the large N550-P900 complex, the N350 deflection still remained apparent. Different scalp topographies were again observed for the different components. N350 tended to be uniformly distributed over mid-line areas of the scalp . It was maximum at Cz declining in amplitude by 30% at Fz and 27% at Pz . These differences did not reach significance. N550 was markedly frontally distributed, declining in amplitude by 32% and 45% at Cz and Pz, respectively ($F < 1$). P900 had a more fronto-central distribution, tending to be maximum at Fz and declining in amplitude by 7% and 46% at Cz and Pz, respectively. These differences were not significant.

---------- Insert Figure 5 here ----------

The effects of tonal frequency on the averaged K-Complex are illustrated in Figure 5. When a K-Complex was observed (left hand portion of the figure), N350 varied in amplitude from 13 to 78 μV in individual subjects or across conditions ($\bar{X}$ = 32.7, SD = 24.6 μV). On these trials, its amplitude was not significantly affected by the frequency (2000, 1000 or 500 Hz) of the stimulus ($F < 1$). Stage of sleep had no main or interacting effects. Its amplitude was reduced by approximately 60% on trials on which no K-Complex could be identified in the background noise. Stage of

sleep had no main or interacting effects. No latency shifts were observed for any of the conditions or in any stage of sleep.

When a K-Complex was elicited, N550 amplitude varied from 47 to 163 μV ($\bar{X}$ = 94.6, SD = 31.2 μV) at Fz. No significant differences were found for either its amplitude ($F < 1$) or its latency ($F < 1$) for the manipulation of the stimulus frequency. When no K-Complex could be identified, N550 was not visible.

The P900 component varied from 13 to 75 μV ($\bar{X}$ = 28.3, SD = 16.5 μV) followed the same pattern as the N550 on trials on which a K-Complex could be identified. Thus, the manipulation of the frequency of the stimulus did not significantly affect the K-Complex's amplitude or latency ($F < 1$ in both cases). On the other hand, on single trials on which a K-Complex could not be identified, only a very small amplitude P900 was visible in the averaged waveform.

Discussion

Across the two experiments, in the "standard" 80 dB 2 ms rise-time conditions, the overall probability of eliciting a K-Complex was approximately 0.50. The probability of eliciting this response decreased with a decrease in stimulus intensity and an increase in rise-time. Although these probabilities were not significantly different, they are consistent with other studies (Halász et al., 1985; Church et al., 1978; Campbell et al., 1985). The second experiment indicated that tonal frequency had

no significant effect on the probability of eliciting the K-Complex, replicating similar findings by Campbell et al. (1985).

In the initial experiment, the K-Complex was elicited more frequently in the first half of the night than in the second. This was not the case in the second experiment where K-Complexes were elicited more often in stage 2 (both early and late) than in SWS. Halász et al. (1985) found that the number of evoked K-Complexes decreased from the early to the later portion of sleep and, furthermore, from cycle to cycle. The probability of elicitating a K-Complex was higher in ascending slopes of sleep stages than in descending ones. They interpreted this as being related to the "deepness" of stages of sleep since K-Complexes were more frequently observed when stage 2 was followed by stage 3-4 than by stage REM. However, some authors (Largo, Leittao, Rosa and Paiva,1991; Halász, Rajna, Kundra, Vargha, Bologh and Kemeny, 1977) have reported a significantly higher density of K-Complexes in the 10 minute time period prior to REM sleep. On the other hand, Paiva and Rosa (1991) have indicated that the frequency of occurrence of a K-Complex does not vary among the stages or cycles of sleep. Our present results thus are in agreement with their findings. Paiva and Rosa (1991) have nevertheless observed that the number of K-Complexes markedly increases in the period prior to *any* stage transition (i.e., not just REM or when the transition is to a "deeper" stage of sleep).

When the K-Complex was elicited, it consisted of a biphasic negative deflection (N350, N550) followed by a late positive

deflection (P900). N350, N550 and P900 were found to have different topographies. These results are in agreement with those obtained by Ujszászi and Halász (1986). They also noted that the N350 component was evenly distributed over midline areas while the N550 component was markedly frontal distributed. Paiva and Rosa (1991) have also reported that the spontaneous K-Complex (N550-P900) was usually distributed frontally or fronto-centrally. In fewer cases, it was distributed maximally at the vertex and in rare cases, over posterior sites. It is possible that differences in scalp topography are due to a comparison of spontaneous versus evoked K-Complexes, peak-to-peak versus baseline-to-peak measurement, or measurement of single trials (and the possibility of overlapping background noise) versus averaged K-Complexes. The P900 was distributed fronto-centrally. When the large N550-P900 could not be discerned in the background noise (i.e., when their peak-to-peak amplitude did not exceed 75 μV), only small amplitude N350 and P900 waveforms were visible following averaging. N550 was not visible in averages of individual subjects or in the grand averages of these individual averages in any stage of sleep. On this basis, it can be concluded that N350, N550 and P900 reflect distinct processes.

Neither the peak amplitude nor latency of N550 or P900 was significantly affected by either the manipulation of stimulus intensity, rise-and-fall time, or tonal frequency. Moreover, their morphology remained unaltered throughout the different stages of sleep. This provides powerful support for the classic

notion that the K-Complex (at least the large amplitude N550-P900 complex) is an all-or-none phenomenon (Roth et al., 1956). An external stimulus will either elicit a K-Complex or it does not. When it does, the N550-P900 complex does not vary in amplitude regardless of manipulation of the parameters of the evoking stimulus. Such findings contradict results obtained by Campbell et al. (1985) and Church et al. (1978) who showed variation in the amplitude of the K-Complex with either manipulation of stimulus intensity or rise-and-fall time. This controversy may be explained by the fact that these previous studies averaged all trials regardless of whether a K-Complex was evoked or not. The indiscriminate use of averaging probably accounted for their effects.

It is possible that the arbitrary decision to select only fronto-central responses exceeding 75 μV might have confounded these results. This does not appear to be the case. When averaged, trials on which N550-P900 did not exceed 75 μV contained no visible evidence of a N550 deflection. On the other hand, it is also possible that on some trials, noise was considered to be a true K-Complex. In such cases, the background noise had to exceed 75 μV in the time interval used to define a K-Complex and moreover, the noise had to have a fronto-central distribution. This was highly unlikely.

Residual background noise can, however, be used to explain the variation in the K-Complex within and between conditions. Although averaging techniques will reduce background noise, it

will not eliminate it altogether. Individual subject averages for a single condition were at times based on a relatively small number of trials (as few as 4 or 5 in some cases), depending on the number of K-Complexes that were elicited. The amplitude of the background noise is reduced in a non-linear asymptotic manner. While the background noise will therefore be markedly reduced after a small number of trials (even with the large amplitude background EEG seen in sleep), a significant amount of noise will remain in the waveform following averaging procedures.

On trials on which the large N550-P900 complex was not identified, N350 was still visible, although markedly reduced in amplitude compared to trials on which N550-P900 was elicited. In these trials, N350 varied directly as a function of the intensity of the stimulus. On the other hand, on trials on which the N550-P900 complex was elicited, N350 was not affected by stimulus intensity. It would thus appear that N350 continues to increase in amplitude with increases in stimulus intensity until it reaches a certain critical threshold amplitude at which point the invariant all-or-none N550-P900 is triggered. As mentioned, neither N550 nor P900 was affected by manipulation of stimulus intensity.

A number of negative waves in the 350-450 ms latency have been reported in the sleeping subject. For example, a late negative wave peaking at about 350 ms increases in amplitude at sleep onset (Ornitz, Ritvo, Carr, La Franchi and Walter, 1967; Ogilvie, Simons, Kuderian, MacDonald and Rustenburg, 1991).

Picton and Hillyard (1988) suggested that a sleep "N2" might play a role in arousing the subject from sleep or alternatively as a means to prevent arousal from it. Others have observed a "vertex sharp wave" at sleep onset, occurring again in the 350-450 ms range following stimulus presentation. Broughton (1988) has suggested that N2 at sleep onset may be related to the presence of vertex sharp waves. It may well be that the sleep-onset N2, the vertex sharp wave and the N350 wave reflect the same process. However, N350 and N2 have different scalp distributions. N2 is markedly frontally distributed while N350 is evenly distributed over midline areas (and tends to be largest at the vertex). Moreover, N2 decreases in amplitude later in the night (Ogilvie et al., 1991; Campbell, McGarry and Bell, 1988) while N350 remains relatively unaltered. In any case, the present findings suggest that N350, while perhaps being part of the K-Complex, is not unique to it. It is possible that N350's role could be limited to the initiation of the N550-P900 complex and it may be this complex that either assists or prevents the arousal from sleep.

Hess (1965) has suggested that the K-Complex (the N550-P900 complex) may play an important role in the prevention of awakenings. Recently, Ujszászi and Halász (1986) claimed that information processed by the K-Complex would provide an indication of non-specific arousal mechanisms and could play an important role in orientation in sleep. In this context, McDonald and Carpenter (1975) reported that the K-Complex can be

elicited to meaningful stimuli (such as the subject's name). Oswald et al. (1960) claimed that the more significant the stimulus (the more it resembled the subject's name), the larger the amplitude of the K-Complex. Oswald et al. (1960) and McDonald and Carpenter (1975) therefore suggested that the K-Complex was an "Orienting Response" (OR). The probability of evoking a K-Complex increases with the intensity of the stimulus (Halász et al., 1985; Church et al., 1978; Campbell et al., 1985). This is also the case with an OR. However, the probability of eliciting a K-Complex also increases with a decrease in the rise-and-fall time of the stimulus. Stimuli that are loud (>100 dB) and abrupt (i.e., having fast rise-times) may evoke a "Defensive Response" (DR) (Berg, Jackson and Graham, 1975). In the present study, stimulus intensity did not exceed 80 dB SPL. This intensity rarely elicits a DR in the waking subject. The effects of loudness might however vary from the waking to the sleeping states. Indeed, Church et al. (1978) have indicated that lower intensity 44 dB SPL tones cause an acceleration in the heart-rate in the sleeping subject. Heart-rate acceleration is considered to be a component of the DR (rather than an OR). It would therefore seem to be possible to elicit DRs with even relatively low intensity stimuli in the sleeping subject. The Johnson and Karpan study (1968) also noted that heart-rate acceleration occurred when K-Complexes did not. From this perspective, while the K-Complex may occur in

association with other indices of a DR, DRs also occur in the absence of the K-Complex.

In conclusion, our results suggest that the K-Complex consists of three components, N350, N550 and P900. These components seem to be morphologically and functionally independent. The three components have different scalp topographies. Moreover, N350 was still apparent on trials in which N550-P900 could not be clearly identified in the background noise. On these trials, the amplitude of N350 varied directly with the intensity of the evoking stimulus. The amplitude of N550-P900 did not vary on trials in which a K-Complex was elicited. This complex therefore appears to be an all-or-none phenomenon.

TABLE 1: Effects of stage of sleep and scalp site on the mean amplitude (in μV) of the different components of the K-Complex (SDs are in parentheses) for the standard condition (80 dB SPL intensity, 2 msec rise-and-fall time).

	2 Early	2 Late	SWS
N350			
Fz	-26.7 (21.9)	-35.5 (28.1)	-38.9 (22.1)
Cz	-28.3 (19.7)	-42.5 (24.6)	-49.3 (23.2)
Pz	-21.5 (17.1)	-26.9 (22.2)	-32.5 (15.0)
N550			
Fz	-67.7 (17.5)	-70.8 (17.4)	-93.9 (37.8)
Cz	-37.4 (15.5)	-46.2 (11.5)	-53.4 (21.2)
Pz	-22.4 (14.8)	-33.5 (8.4)	-33.2 (10.4)
P900			
Fz	36.6 (25.5)	38.9 (13.6)	69.1 (18.9)
Cz	28.6 (21.7)	28.6 (12.1)	54.3 (20.9)
Pz	19.3 (13.3)	15.5 (8.8)	39.0 (10.1)

TABLE 2: The effects of stimulus intensity on the mean amplitude (in μV) of the different components of the K-Complex (SDs are in parentheses). Data are from frontal recordings.

	80 dB			60 dB		
	2 Early	SWS	2 Late	2 Early	SWS	2 Late
N350	-26.8 (21.9)	-38.9 (22.1)	-35.5 (28.1)	-14.4 (4.7)	-28.4 (17.5)	-42.0 (32.7)
N550	-67.7 (17.5)	-93.9 (37.8)	-70.8 (17.4)	-68.6 (33.1)	-82.1 (23.9)	-78.4 (33.8)
P900	36.6 (25.5)	69.1 (18.9)	38.9 (13.6)	38.4 (30.2)	33.2 (21.8)	69.2 (20.2)

TABLE 3: The effects of tonal frequency (in Hz) on the mean amplitude (in μV) of the different components of the K-Complex (SDs are in parentheses). Data are from frontal recordings.

	500			1000			2000		
	2 Early	SWS	2 Late	2 Early	SWS	2 Late	2 Early	SWS	2 Late
N350	-50.1	-22.1	-29.9	-33.6	-32.7	-25.3	-12.8	-10.1	-19.2
	(38.6)	(49.9)	(45.8)	(28.6)	(37.8)	(34.4)	(14.8)	(12.9)	(25.1)
N550	-116.6	-82.9	-118.7	-104.3	-86.1	-122.2	-110.3	-71.2	-95.1
	(19.3)	(31.2)	(33.5)	(27.2)	(30.1)	(23.2)	(24.2)	(17.9)	(18.6)
P900	39.4	27.8	24.1	22.5	32.9	24.1	19.1	40.5	13.5
	(10.5)	(11.5)	(11.5)	(13.9)	(5.2)	(22.7)	(17.3)	(15.5)	(19.2)

Figure Legends

Figure 1. The effect of high and low pass filters on single trial (left) and averaged (right) K-Complexes from one subject (AB). The plotted waveforms are from frontal recordings. For this subject, the "average" on the right-side of the figure is the average of 14 single trials containing a K-Complex. In five channels, the high filter was held constant at 15 Hz but the time constant was varied, being either 5.0, 2.0, 1.0, 0.3 or 0.1 s. In the other three channels, the time constant was held constant at 1 s and the high filter settings were varied being either 35, 70 or 500 Hz. In both the single trial and averaged waveforms, a time constant below 1 s resulted in the attenuation of the large negative wave at approximately 500 ms and of a late slow wave in the 1000 - 1500 ms interval. High frequency background noise can be observed in filter settings above 35 Hz.

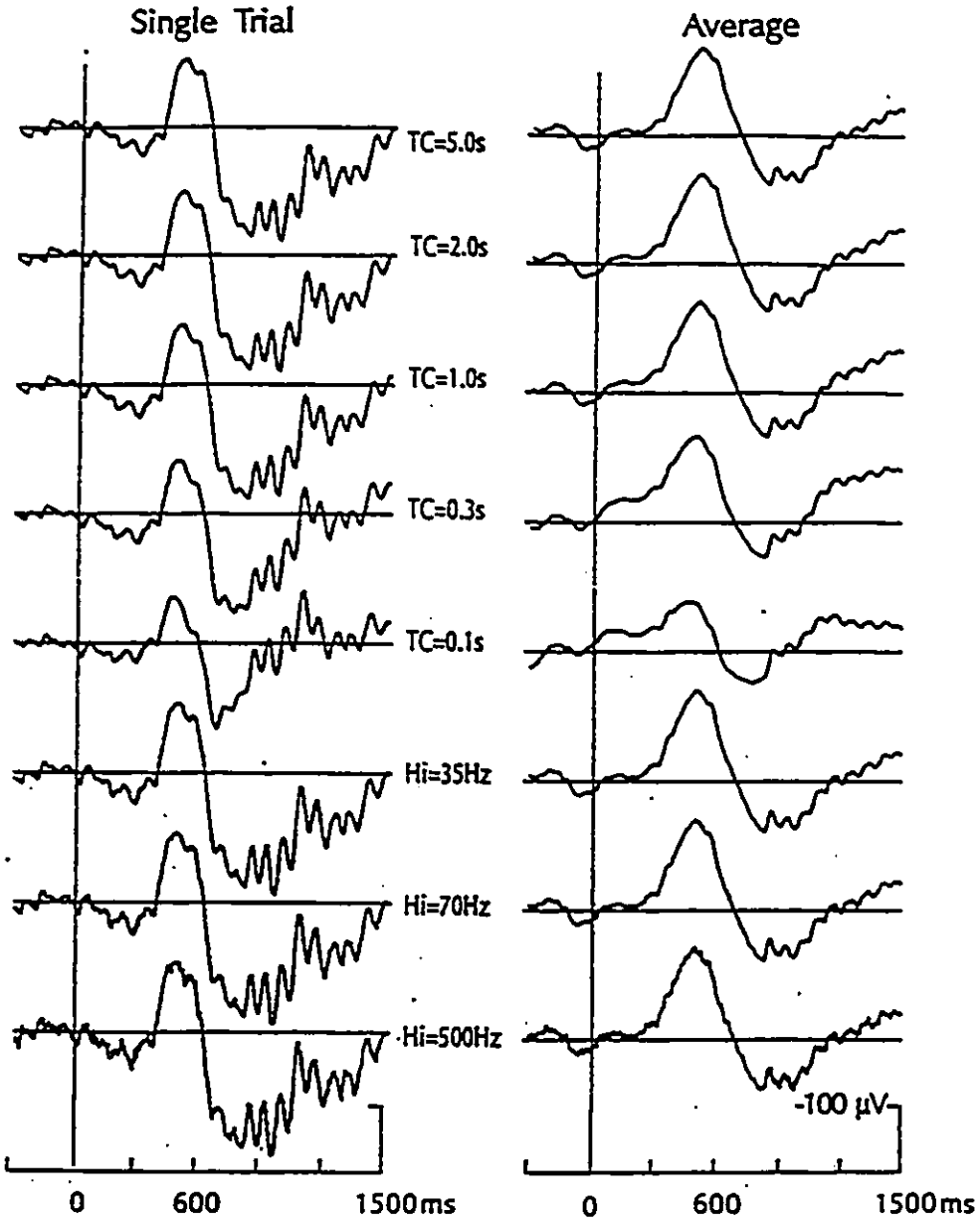
Figure 2. Single trials obtained from one subject (DC) for the standard condition on trials on which a K-Complex could (left) and could not (right) be elicited. The recordings were obtained during SWS where background activity is especially apparent. The average of these single trials is presented at the bottom of the figure. As can be seen, the average is a good reflection of the single trials.

Figure 3. Grand Averages (average of all subjects' averages) on each of the nine trials for the Standard condition during early stage 2 sleep. No sequential effects were observed for the probability of occurrence of a K-Complex within the nine consecutive trials. Furthermore, neither the amplitude nor the latency of the various components of the K-Complex varied significantly.

Figure 4. Grand Average of all subjects for all trials containing (left) and not containing (right) a defined K-Complex. Note that trials on which a K-Complex could not be discerned are plotted at a gain of x 4. Stimulus intensity was either 80 (thick line) or 60 dB (thin line). The K-Complex consist of an early negative peak "N350", a second negative peak "N550" and followed by a positive peak "P900". N350 remains visible (although attenuated) while N550 is difficult to discern and P900 is markedly attenuated on single trials on which a K-Complex could not be identified.

Figure 5. Grand Average of all subjects for all trials containing (left) and not containing (right) a defined K-Complex. Note that trials on which a K-Complex could not be discerned are plotted at a gain of x 4. Tonal frequency was either 500 (thin line), 1000 (medium line) or 2000 Hz (thick line). Again, the K-Complex consist of an early negative peak "N350", a second negative peak "N550" and followed by a positive peak "P900". N350 remains visible (although attenuated) while N550 is

difficult to discern and P900 is markedly attenuated on single trials on which a K-Complex could not be identified.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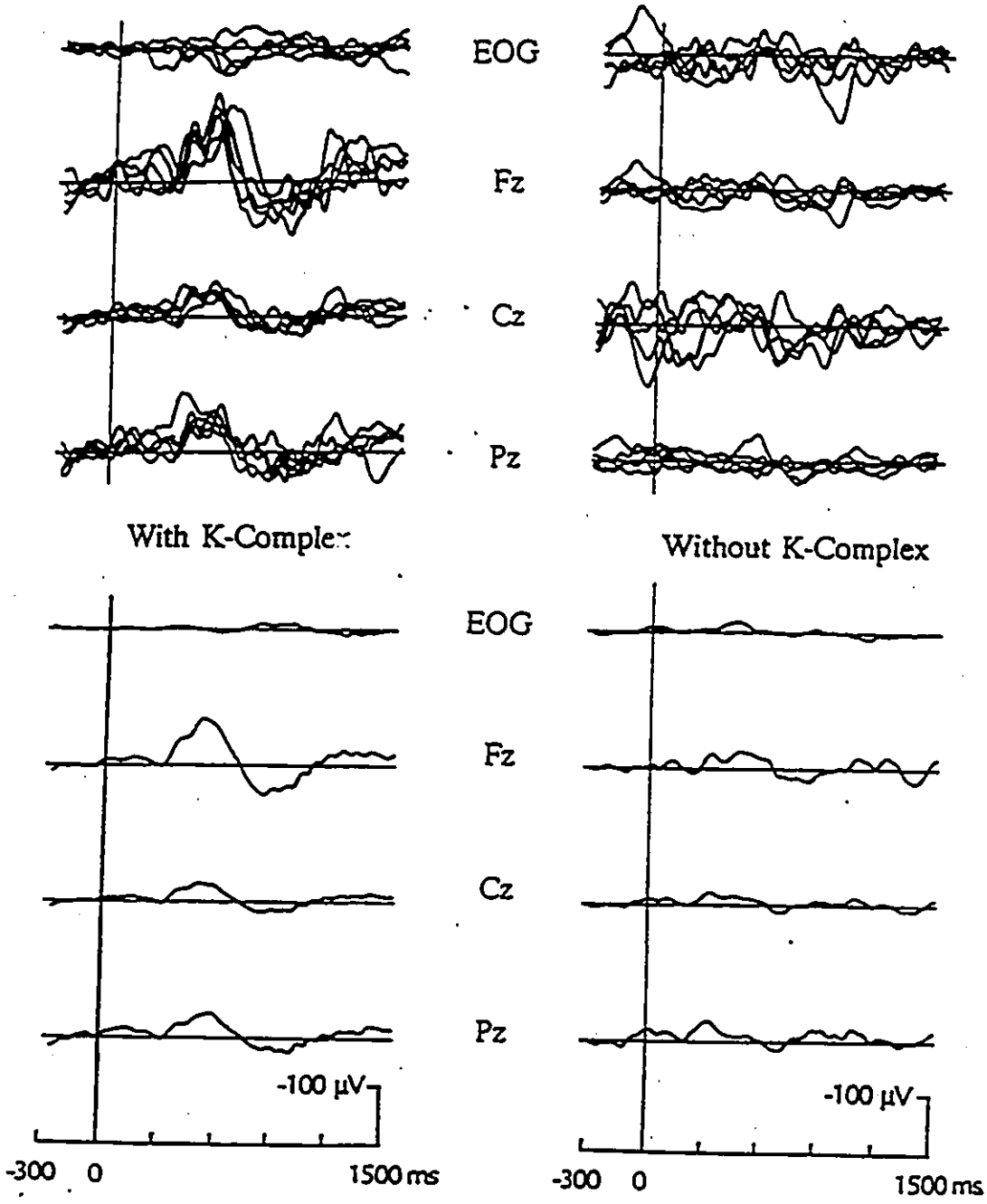
EOG
Fz
Cz
Pz
With K-Complex
Without K-Complex
EOG
Fz
Cz
Pz
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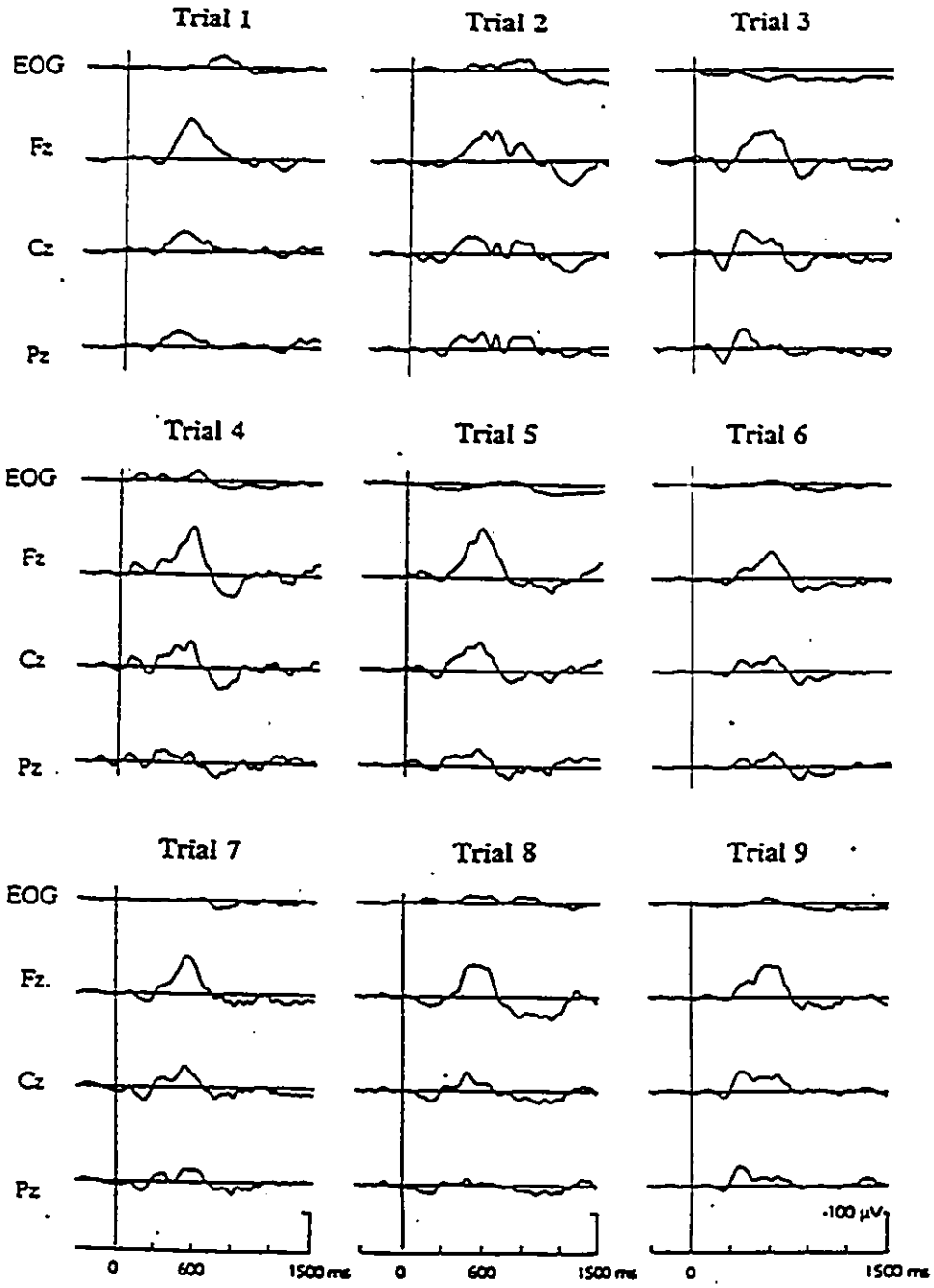
1500 ms


Trial 1
Trial 2
Trial 3
EOG
Fz
Cz
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Trial 4
Trial 5
Trial 6
EOG
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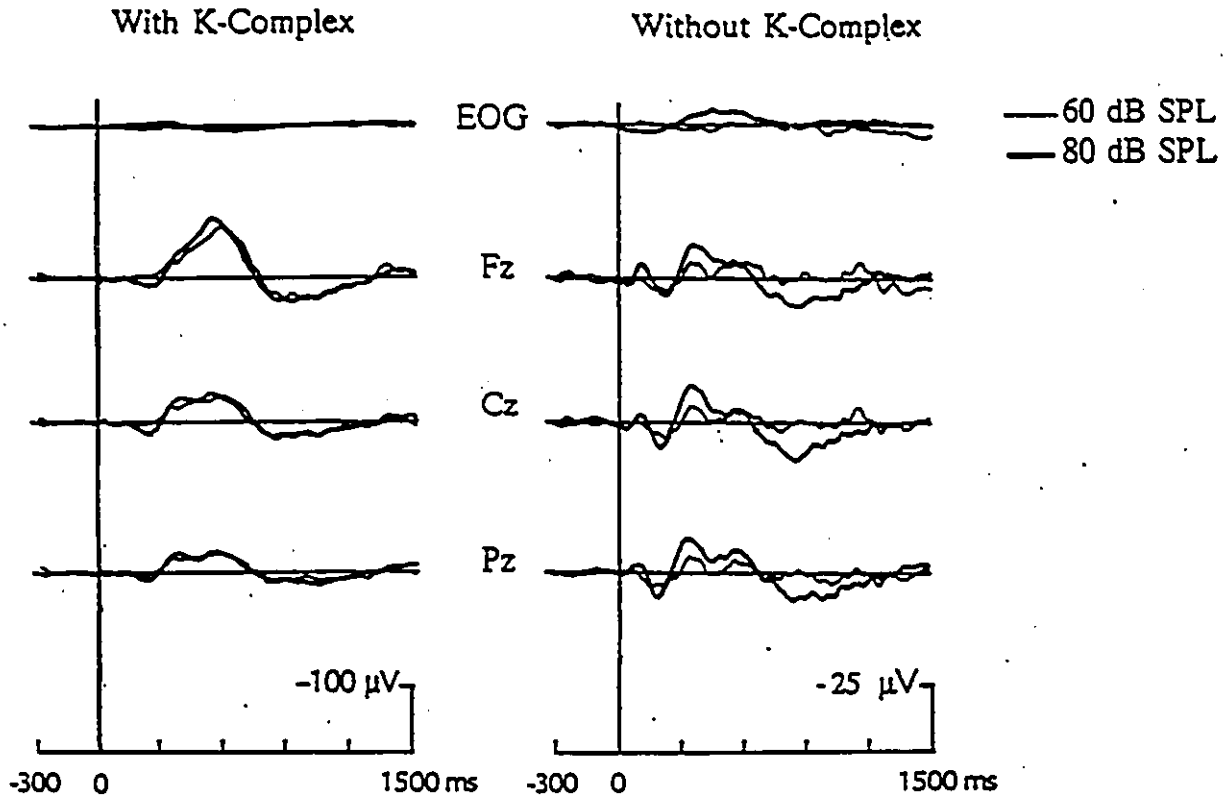
With K-Complex
Without K-Complex
EOG
Fz
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Pz
60 dB SPL
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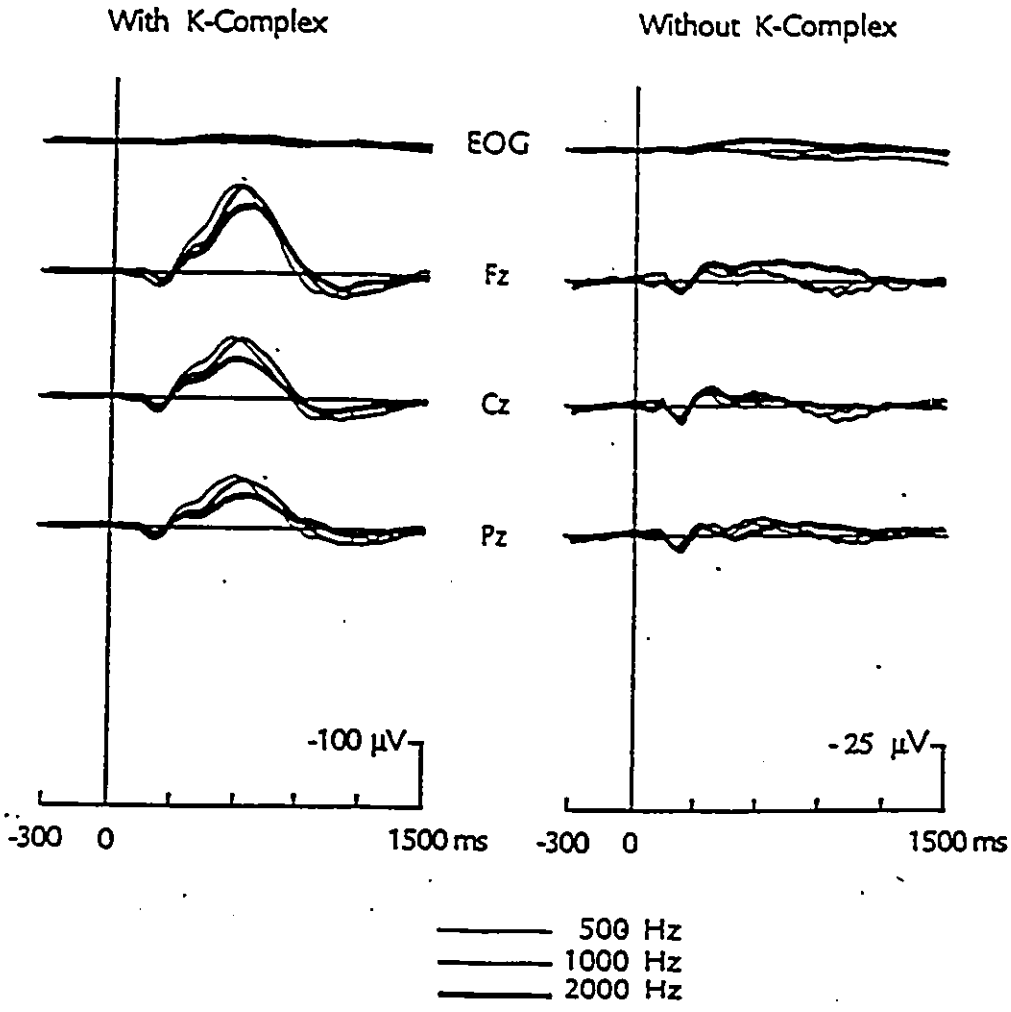
1500 ms


With K-Complex
Without K-Complex
EOG
Fz
Cz
Pz
-100 µV
-25 µV
-300
0
1500 ms
-300
0
1500 ms
500 Hz
1000 Hz
2000 Hz

Chapter 3

Experiment 2

Effects of rate of stimulus presentation on the evoked K-Complex.

Introduction

The K-Complex consists of a well-delineated negative wave peaking at approximately 550 msec (N550) followed by a positive wave peaking at approximately 900 msec (P900). An earlier negative component peaking at about 350 msec (N350) has also been considered to be part of the K-Complex by some authors (Halász, Pal and Rajna, 1985; Ujszászi and Halász,1986). Most studies (Roth et al., 1956; Oswald, Taylor and Treisman, 1960) have nevertheless considered the K-Complex to be a single functional entity. The K-Complex occurs spontaneously and may also be elicited by an external stimulus (Loomis, Harvey and Hobart, 1939) during stages 2, 3 and 4 of sleep (Davis, Davis, Loomis, Harvey and Hobart, 1939; Roth, Shaw and Green,1956). It cannot be elicited during REM sleep.

There is now good evidence to suggest that in fact the K-Complex consists of at least three distinctive "components". The definition of a "component" (as opposed to "peak" or "deflection" of an evoked potential) varies amongst authors. For some (e.g., Näätänen and Picton, 1987), independent components must have different intracranial generators. For others (e.g., Donchin et al., 1986), independence of a component can be determined on the basis of either experimental manipulations (the manipulation

affects one component but not another) or statistical independence (for example, following principal component analysis, a "component" is not correlated with another component). The different peaks of the K-Complex have different scalp topographies indicating that they must have different intracranial generators (Bastien and Campbell, 1992). Moreover, the experimental manipulations affected the three peak deflections in different ways.

The functional role of the K-Complex remains controversial. Hess (1965) speculated that the K-Complex reflected a process that protects the brain from unnecessary arousal. On the other hand, others, such as Church, Johnson and Seales (1978), have considered the K-Complex to be an arousal reaction. In this regard, Oswald et al. (1960) reported that the K-Complex varied with the psychological salience of the stimulus (the more significant the stimulus, the larger the K-Complex). In an earlier study, Roth et al. (1956) reported that the K-Complex was unaffected by the manipulation of the physical qualities of simple stimuli, such as tones or clicks. In their study, Bastien and Campbell (1992) presented auditory stimuli to the sleeping subject. Certain of these stimuli elicited a K-Complex while others did not. They then sorted out trials containing and not containing a K-Complex. Averaging techniques were used to remove background noise. When a K-Complex was evoked, the amplitude and latency of the N550 and P900 components remained unaltered despite manipulations of stimulus intensity, tonal frequency and

rise-and-fall time. The N550-P900 appeared to be an "all-or-none" phenomenon.

Bastien, Campbell and Rouillard (1991) measured the amplitude of consecutive occurrences of the K-Complex. Stimuli were presented in blocks of 9 consecutive trials. The inter-trial interval (i.e., the time between each of the 9 stimuli) was 10 sec. The time between blocks varied from 1 to 2 minutes. Within any block, the occurrence of 3 consecutive K-Complexes was identified. The amplitude of the K-Complex was larger for the first occurrence of the K-Complex than for the second or third occurrence. Two possible interpretations for this reduction in the amplitude were offered. The gradual decay could be a reflection of an habituation process. Alternatively, it could be a reflection of the refractory period. The length of time between the last occurrence of a K-Complex and its subsequent initial reoccurrence was at least 20 sec and usually considerably longer. Thus, the time from the last to the initial K-Complex was considerably longer than from the initial to the second K-Complex.

The refractory period of the K-Complex was therefore estimated to be at least 10 sec. This is in conflict with earlier reports. The refractory period of the K-Complex was estimated to be around 3 sec by Roth et al. (1956). Bancaud, Block and Paillard (1953) reported that the refractory period of the K-Complex was a very short 300 msec. Differences in methodology in the recording and scoring of K-Complexes could

account for these discrepancies. In these earlier studies, the determination of the refractory period was based on the presence or absence of a single K-Complex. The actual amplitude of the single trial K-Complex was rarely measured. The K-Complex occurs in NREM sleep, a period in which the amplitude of the background EEG may be exceedingly large. This background EEG (or "noise") overlaps and may sum with the single trial K-Complex. Trial-to-trial variation of the amplitude of the K-Complex could be due to variation in its actual amplitude or to variation in the amplitude of the background noise. Bastien et al. (1991) and Bastien and Campbell (1992) used signal averaging techniques to attenuate background noise.

A factor long-known to affect the likelihood of eliciting a K-Complex is the rate of stimulus presentation (Roth et al., 1956). Recently, Kurella, Heitman, Golz and Dormann (1992) have indicated that the probability of eliciting a K-Complex increases as the ISI becomes longer. The present study was designed to systematically determine the effects of rates of stimulus presentation on the amplitude of the evoked K-Complex. In different conditions, the rate of stimulus presentation was varied. Trials were sorted according to those on which a K-Complex could be identified and on those on which a K-Complex could not be identified. Signal averaging techniques were employed to reduce the amplitude of the background EEG.

Methods

Subjects

Ten young adults (5 males, 5 females) between the ages of 20 and 35 ($\bar{X}$ = 23) were tested in a single all-night session. All subjects reported normal hearing. None reported neurological, psychiatric or sleep disorders. They were instructed to refrain from alcohol and drug use for 24 hours prior to the experiment. All subjects were asked to read and sign a consent form that provided details of the experimental paradigm and procedures. Each subject received an honorarium for their participation in the study.

EEG Recording

The EEG was recorded with Grass gold cup electrodes placed at midline frontal, central and parietal sites (Fz, Cz, and Pz) referenced to the left mastoid. The EOG was recorded with electrodes fixed at the supra-orbital ridge of one eye and the infra-orbital ridge of the other. This permitted the recording of horizontal and vertical eye movements on a single polygraphic channel. Inter-electrode impedance was maintained below 5 kOhms.

Procedure

Each subject was individually fitted with a hearing-aid/ear mould device through which the auditory stimuli were presented. The hearing-aid system assured constancy of stimulus input

despite changes in head position during the night (Campbell and Bartoli, 1986). Stimuli were 80 dB SPL, 2000 Hz tone pips having a total duration of 52 msec and a 2 msec rise-and-fall time. Bastien and Campbell (1992) indicated that such stimulus characteristics were optimal for eliciting a K-Complex. Stimuli were presented in blocks of 40, 20 or 10 trials depending on the ISI used. The time between blocks was 2 minutes. The ISI was varied in different conditions. In the Short, Medium and Long conditions, the ISI was either 5, 10 or 30 sec respectively.

EEG Analysis

The different stages of sleep were classified on-line by an experienced rater according to standard scoring criteria (Rechtschaffen and Kales, 1968). Testing occurred during definite stage 2, 3, and 4 sleep. Stage 2 was subdivided into early (2E) and late (2L) halves of the sleep period to examine possible time-of-nights effects. Stages 3 and 4 were combined to form slow wave sleep (SWS). In the rare cases of stage classification ambiguity (less than 5% of conditions), records were later scored by a second, experienced rater. If the raters disagreed, the condition was rejected from further analysis. Stimulus presentation was discontinued and rejected when the EEG pattern showed signs of a stage change or upon subject movement.

EEG analysis began 300 msec prior to stimulus onset and continued for the following 1500 msec (i.e., the total sweep time was 1800 msec). A total of 256 data points were digitized for

each channel (i.e., the dwell time was once every 7 msec). The average of the pre-stimulus activity served as baseline from which peak deflections were measured.

Single trials were sorted according to those on which a K-Complex was identified and those on which a K-Complex could not be identified (for this purpose, the K-Complex was defined according to Rechtschaffen and Kales (1968) criteria as a negative-positive complex having a negative peak between 450 and 650 msec and a positive peak between 700 and 1200 msec with an overall peak-to-peak amplitude of at least 75 μV [1]). The sorted trials were then averaged to reduce background activity. The averaging procedure is illustrated in Figure 1.

---------- Insert Figure 1 here ----------

Single trials containing a K-Complex are shown in the top portion while trials not containing a K-Complex are shown in the bottom portion of Figure 1. Single trials are shown in the left-hand column while the average of these trials is shown in the right-hand column. As may be observed, the average is a good representation of the single trials, although there is considerable background noise that contributes to inter-trial variability. The single trial waveforms in this figure were recorded from a single subject.

Data Analyses

N350 was defined as the maximum negative peak in the 300-450 msec range, N550 as the maximum negative peak in the 450-700 msec range and P900 as the maximum positive peak in the 700-1200 msec range. The latencies and amplitudes of N350, N550 and P900 served as dependent measures. A 3-way ANOVA was conducted with repeated measures on ISI (Short, Medium, Long), scalp site (Fz, Cz, Pz), stage of sleep (2 early, SWS, 2 late) on trials on which a K-Complex could be identified and when it could not be identified. The analyses were carried out using the BMDP2V procedure with Wilk's Lambda employed to test for sphericity. Previous research (Kurella et al., 1992) has indicated that the probability of eliciting a K-Complex increases as the ISI becomes longer. For this reason, multiple one-tailed t-tests were also run to assess differences in the probability of occurrence of K-Complexes across conditions. For all comparisons, the significance level was set at $p < .05$.

Results

A K-Complex was evoked on approximately 50% (mean across subjects) of all trials. K-Complexes were elicited more often in stage 2E and 2L (.56 and .51, respectively) than in SWS (.48), although the differences were not significant. They occurred significantly more often when the ISI was 30 sec (.62) compared to when it was either 10 or 5 sec (.53 and .38, respectively; $t(19) = -1.72$ and 5.57, respectively; $p < .05$ in both cases).

The difference between the 10 and 5 sec ISIs was also significant ($t(22) = 5.11$, $p < .05$). Percentages of trials on which K-Complexes were elicitated for each condition and sleep stage are reported in Table 1.

---------- Insert Table 1 here ----------

Grand averaged (the average of the averaged evoked potential of all subjects) waveforms are illustrated in Figure 2. They are sorted according to the presence or absence of a K-Complex across the different conditions.

---------- Insert Figure 2 here ----------

Trials with a K-Complex

As may be observed in the left-hand portion of Figure 2, the K-Complex consisted of double-negative N350-N550 deflections followed by a later positive P900 deflection.

N350 varied in amplitude between 20 and 80 μV on trials on which a K-Complex was observed. N350 was larger at the central compared to the frontal and parietal sites ($F(2,18) = 10.82$, $p < 0.05$). There was no interaction with stages of sleep and N350 did not vary significantly in amplitude or latency across the different stages of sleep ($F < 1$). On trials on which a K-Complex was observed, a main effect of the N350 amplitude was observed for the Short and Medium compared to the Long ISI

condition ($F(2,18) = 13.84$, $p < 0.05$). Stage of sleep did not alter this difference.

N550 varied in amplitude from 50 to 200 μV in trials in which a K-Complex could be observed. A main effect of electrode site was observed, N550 amplitude being maximum at Fz and declining in amplitude at Cz and Pz ($F(2,18) = 48.81$, $p < 0.05$). No interaction was found with the different stages of sleep. N550 peaked earlier in SWS ($F(2,18) = 4.94$, $p < 0.05$) than in either the early or late portions of stage 2. Although N550 peaked earlier in the Long condition than in the Medium and Short conditions, differences only tended toward significance. A main effect of rate of presentation was observed for the amplitude of N550. It was significantly larger when the rate of presentation was 30 sec ($F(2,18) = 3.97$, $p < 0.05$) than when it was 10 or 5 sec. Again, the different stages of sleep did not alter this phenomenon.

P900 varied in amplitude between 15 and 70 μV in trials in which a K-Complex could be observed. P900 latency did not vary across the different stages of sleep ($F < 1$). Although P900 peaked earlier in the Long condition than in the Medium or Short ones, these differences were not significant ($F < 1$). P900 amplitude was larger in SWS than in 2E and 2L ($F(2, 18) = 4.16$, $p < 0.05$). Like N350 and N550, P900 was significantly larger when the rate of presentation was 30 sec than when it was 10 or 5 sec ($F(2,18) = 4.26$, $p < 0.05$).

Trials without a K-Complex

On trials on which a K-Complex could not be identified (i.e., when N550-P900 peak-to-peak amplitude did not exceed 75 μV, right-hand portion of Fig 2), a positive wave peaking at about 250 msec followed by a negative wave at 350 msec was still visible. The later N550-P900 complex could not be discerned in the background noise of the averaged waveform. On trials on which the K-Complex was not observed, neither the latency nor the amplitude of N350 was affected by the different stages of sleep or the rate of presentation of the stimulus ($F < 1$).

Analysis of Consecutive K-Complexes

Differences in the K-Complex were observed as a function of the ISI. This could be due to refractory processes or, alternatively, it is possible that the effects could be explained by habituation processes (the K-Complex habituated more rapidly during rapid stimulus presentation). To test this possibility, trials on which 3 consecutive K-Complexes were elicited were compared. Three-way repeated measures ANOVAs were run for the comparison of the ordinal position of the K-Complex (First, Second, Third) within each of ISI condition for each stage of sleep. The analyses were carried out using the BMDP2V procedure using Wilk's Lambda to test for sphericity and Greenhouse-Geisser corrections employed when appropriate.

The procedure for selection of trials is illustrated in Figure 3. In these simulated data, in the first block of nine

trials, a K-Complex is visible on the first, second and third trials; in the second block of nine trials, a K-Complex is visible on the fifth, sixth and seventh while on the n^{th} block, a K-Complex is visible on trials 7, 8 and 9. In block 1, a possible K-Complex is apparent on trials 5 and 6 and perhaps on trial 7. However, on trial 7, its amplitude did not exceed the minimum 75 μV peak-to-peak criterion. Since 3 consecutive K-Complexes could not be identified, trials 5 and 6 would be rejected from further analysis. The K-Complexes were then averaged according to ordinal position such that within a particular stage of sleep all first occurrences were averaged with the subsequent first occurrences, second consecutive occurrence averaged with other subsequent second occurrences and third consecutive occurrences averaged with other subsequent third occurrences.

---------- Insert Figure 3 here ----------

Figure 4 presents grand averages of all subjects for whom a K-Complex was elicited on three consecutive trials during the Short, Medium and Long ISI conditions. There was no main effect of sequential order or ISI on the latency of N350, N550 or P900 ($F < 1$ in all cases). Similarly, there was no interaction of Order and ISI on the latencies of the different peaks ($F < 1$). In all ISI conditions, there was no interaction with stage of sleep for any component ($F < 1$ in all cases). A main effect of

the order of presentation could be observed for the amplitude of N350 and N550 in the Short ISI condition ($F(2,18) = 11.78$ and 11.72, $p < 0.05$, respectively). N350 and N550 were attenuated by approximately 50% and 30% respectively, on the second and third trials when compared to the first. P900 was not affected by sequential order ($F < 1$). A main effect of the order of presentation could also be observed for the amplitude of N550 in the Medium ISI condition ($F(2, 18) = 3.97$, $p < 0.05$). In this condition, N550 was attenuated by approximately 20% on the second and third trials when compared to the first. N350 and P900 were not affected by the order of presentation of the stimulus ($F < 1$). No significant differences for the amplitude of the different components were observed for the Long ISI ($F < 1$). Again, stages of sleep did not alter this phenomenon.

---------- Insert Figure 4 ----------

Discussion

K-Complexes were elicited more often when the ISI was longer (30 sec) than when it was shorter (5 and 10 sec). Moreover, N350 and N550 amplitudes were larger in the Long compared to the Medium and Short conditions. Their attenuation under the fastest rates of presentation could be interpreted as an habituation process. The K-Complex might have habituated more rapidly in the Short and Medium conditions than in the Long condition. Supporting this interpretation are the data from the consecutive

K-Complex data. When three consecutive K-Complexes were elicited, the amplitude of N350 and N550 decreased upon repetition of the stimulus under the Short and Medium ISIs. There was no effect of repetition in the 30 sec ISI condition. On average, therefore, N350 and N550 were attenuated in the Short and Medium conditions compared to the Long.

There is some evidence in the literature that the K-Complex might serve as an orienting response (OR) during sleep. The elicitation of an OR occurs upon the recognition of a novel or significant stimulus. As such, the OR must involve a memory comparison process. McDonald, Schicht, Frazier, Shallenberger and Edwards (1975) reported that the K-Complex can be elicited by meaningful stimuli (such as the subject's name). Oswald et al. (1960) claimed that the more significant the stimulus (the more it resembled the subject's name), the larger the amplitude of the K-Complex. Oswald et al. (1960) and McDonald and Carpenter (1975) therefore suggested that the K-Complex was an OR. Ujszászi and Halász (1986) also claimed that the K-Complex could play an important role in orientation during sleep.

One of the characteristics of the OR is that it is subject to habituation. The Sokolov (1963) model of habituation assumes that the more often a stimulus is repeated, the less information needs to be extracted from it since it has already been incorporated into a "neuronal model". The magnitude of the OR therefore is reduced upon repetition of the stimulus. This reduction in the OR with repetition is the habituation process.

Responses that are said to have habituated are marked by a gradual decline in amplitude followed eventually by a complete failure to respond (Thompson and Spencer, 1966). This type of pattern has not been observed for the K-Complex. The K-Complex may be elicited for a few consecutive trials and then cannot be elicited at all, followed by an apparent return to full amplitude, perhaps followed again by a complete failure to elicit it, then perhaps another return to full amplitude.

A decline in the amplitude of a response upon repetition of the stimulus is not necessarily due to habituation. Graham and Hackley (1991) have outlined 9 criteria that need to be met for a gradual decline in response amplitude to be due to the habituation process. They specified that decrements should 1) be progressive within a series; 2) be progressive between series; 3) increase with faster repetition rates (criterion later modified); 4) relate inversely to intensity (criterion later modified); 5) generalize to other stimuli; 6) recover spontaneously with time; 7) recover more slowly if repetitions continue beyond zero responding (criterion later modified); 8) dishabituate after insertion of another, usually strong, stimulus; and, 9) reappear with repetition of a dishabituating stimulus (habituation of dishabituation).

The attenuation of the response upon repetition of the stimulus satisfies the first criterion. It is difficult to test a decline across different series. Such an assumption assumes that the subject's state of arousal remains constant. This is

almost certainly not the case during sleep. The third criterion -- that habituation is faster with faster rates of presentation -- does appear to have been met in the present study. Habituation was apparent with faster but not slower rates of presentation. The fourth criterion does not appear to apply to the K-Complex. Bastien and Campbell (1992) noted that manipulation of stimulus intensity did not affect the amplitude of the N550-P900 complex of the evoked K-Complex. There is a paucity of data in the literature to permit a systematic evaluation of criteria 5, 6 and 7. It is known, however, that the K-Complex can be generalized to different stimulus modalities and parameters (Roth et al., 1956), that it recovers spontaneously with time and, that even after continuous stimulation, the K-Complex will spontaneously reappear. Finally, the eighth and ninth criteria, concerning dishabituation, have not been tested. Indeed, it might be impossible to study dishabituation of the K-Complex. A K-Complex cannot be elicited on every trial, even when conditions appear to be optimal for its elicitation (Bastien and Campbell, 1992). Given the typical pattern of responding, a decrement in the response followed by an eventual failure to respond, and then followed by a recovery elicited by a novel stimulus would not necessarily indicate dishabituation. The reason dishabituation is critical is that a gradual decline in amplitude could also be due to refractory effects. If the decline is due to refractory processes, unlike the case with dishabituation, the introduction of a novel stimulus will not result in a return of the response

to baseline levels (Thompson and Spencer, 1966; Roemer, Shagass and Teyler, 1984). Therefore, while the decline in amplitude of N350 and N550 might be evidence in support of habituation, it could also equally be a result of refractory processes. The N350 and N550 were reduced in amplitude during the Short and Medium related to the Long ISI condition. The refractory period for the K-Complex must therefore be between 10 and 30 sec. In support of this hypothesis, the analysis of consecutive K-Complexes also revealed an attenuation in the amplitude of N350 and N550 in the Short and Medium conditions while these components remained unaffected in the Long condition. However, P900 was not altered by any of the rate of presentation of the stimulus, suggesting that its refractory period may be shorter than the refractory period of the N350 and N550 components.

The refractory period for N350 and N550 would be unusually long. Psychological refractory periods (as distinguished from the refractory period of a neuron) can however be extremely long. For example the refractory period of a late positive wave of the event-related potential, P300, has been estimated to be more than 12 sec (Polich, 1990; Fitzgerald and Picton, 1983). P300 has been suggested to index the updating of working memory in waking subjects (Donchin et Coles, 1988), The fact that the recovery period of the K-Complex is long (> 10 seconds) is thus not atypical, assuming its function is psychological in nature.

While many studies have discussed the K-Complex in terms of an OR, others have suggested that it might be a Defensive

Response (DR). The probability of evoking a K-Complex increases with the intensity of the stimulus (Berg, Jackson and Graham, 1975; Oswald et al., 1960; Bastien and Campbell, 1992) and, in some studies, with faster tone rise-and-fall times (Berg et al., 1975; Bastien and Campbell, 1992). Stimuli that are loud and abrupt (i.e., having fast rise-times) may evoke a DR (Graham, 1979). Following a DR, the heart rate accelerates whereas following an OR it decelerates (Church, Johnson and Seales, 1978). Johnson and Karpan (1968) reported increases in heart rate following the occurrence of evoked K-Complexes. This is consistent with the notion that the K-Complex acts as a DR. Furthermore, the DR is differentiated from the OR in that it is not subject to habituation. As already mentioned, the decline in amplitude with repetition of the stimulus that was observed in the present study may be more related to refractory rather than habituation processes. Others have also suggested that the K-Complex should be best considered a DR (Berg et al., 1975; Campbell, Bell and Deacon-Elliott, 1985). However, there are problems with the DR hypothesis. DRs are elicited by loud, abrupt stimuli. The loudest stimulus used in the present study, 80 dB SPL, is well below the minimum level considered necessary to elicit a DR in awake subjects (Graham, 1979). However, Bastien and Campbell (1992) pointed out that it is quite possible that what is considered to be loud for the awake and alert subject may be quite different than for a subject who is

sleeping. The threshold for eliciting a DR might therefore be considerably lower during sleep.

Footnote

[1] In this and other studies carried out in our laboratory, a 75 μV amplitude cut-off has been selected for definitional purposes. Some have commented that this cut-off point is arbitrary. Obviously, some sort of "arbitrary" cut-off will be required in order to exclude random EEG activity being considered as a K-Complex. It is possible that these criteria will exclude K-Complexes whit amplitudes less than 75 μV. If this were the case, the average of these "no K-Complex" trials should in fact reflect this small amplitude waveform. Bastien and Campbell (1992) have indicated, however, that the average amplitude of N550 on these trials is essentially zero. A small (less than 10 μV) P900 does admittedly remain visible. Even granting that a small P900 does occur on "no K-Complex" trials, it would be impossible to detect a single trial 10 μV response in the massively larger background EEG.

Table 1: Percentage of evoked K-Complexes as a function of the ISI and stage of sleep (SDs are in parentheses).

Rate of Presentation	2 Early	SWS	2 Late	Total %
5 seconds	42.5 (14.4)	38.7 (14.4)	31.4 (13.4)	37.5
10 seconds	57.1 (18.6)	50.1 (14.4)	53.0 (21.2)	53.4
30 seconds	62.8 (21.8)	57.8 (21.3)	66.0 (18.3)	62.2
Total %	54.1	48.8	50.1	51.0

Table 2: Effects of rate of presentation of the stimulus on the mean amplitude (in μV) of the different components of the K-Complex (SDs are in parentheses) across scalp sites.

		30 sec	10 sec	5 sec
N350	Fz	-53.3 (28.3)	-24.3 (16.3)	-29.2 (12.6)
	Cz	-57.3 (24.1)	-28.3 (14.7)	-31.3 (12.8)
	Pz	-35.5 (12.9)	-20.6 (12.7)	-21.7 (12.7)
N550	Fz	-115.3 (52.8)	-91.5 (26.0)	-96.9 (28.4)
	Cz	-86.1 (40.8)	-74.3 (28.9)	-75.1 (28.5)
	Pz	-66.3 (38.8)	-55.6 (20.5)	-54.8 (26.2)
P900	Fz	35.6 (18.8)	25.0 (20.2)	25.7 (16.1)
	Cz	34.8 (21.3)	27.1 (14.9)	24.9 (12.2)
	Pz	21.6 (14.3)	17.6 (12.5)	16.5 (11.8)

Table 3. The effects of rate of presentation (in sec) on the mean amplitude (in μV) of the differer components of the K-Complex (SDs are in parentheses)[a]

	5			10			30		
	2 early	Slow-Wave Sleep	2 late	2 early	Slow-Wave Sleep	2 late	2 early	Slow-Wave Sleep	2 late
N350	-33.5 (23.0)	-27.9 (24.0)	-26.1 (14.8)	-18.8 (12.8)	-40.9 (16.8)	-20.6 (16.3)	-50.3 (30.4)	-63.0 (32.8)	-46.5 (24.9)
N550	-117.1 (46.4)	-85.9 (20.0)	-95.6 (44.1)	-95.4 (34.1)	-90.2 (32.2)	-88.7 (56.64)	-118.7 (66.5)	-105.2 (32.6)	-102.9 (38.0)
P900	22.1 (18.0)	39.8 (24.2)	14.9 (9.8)	22.1 (18.0)	37.8 (25.8)	18.1 (4.0)	33.3 (14.7)	45.1 (20.7)	26.3 (14.8)

[a] Data are from frontal recordings.

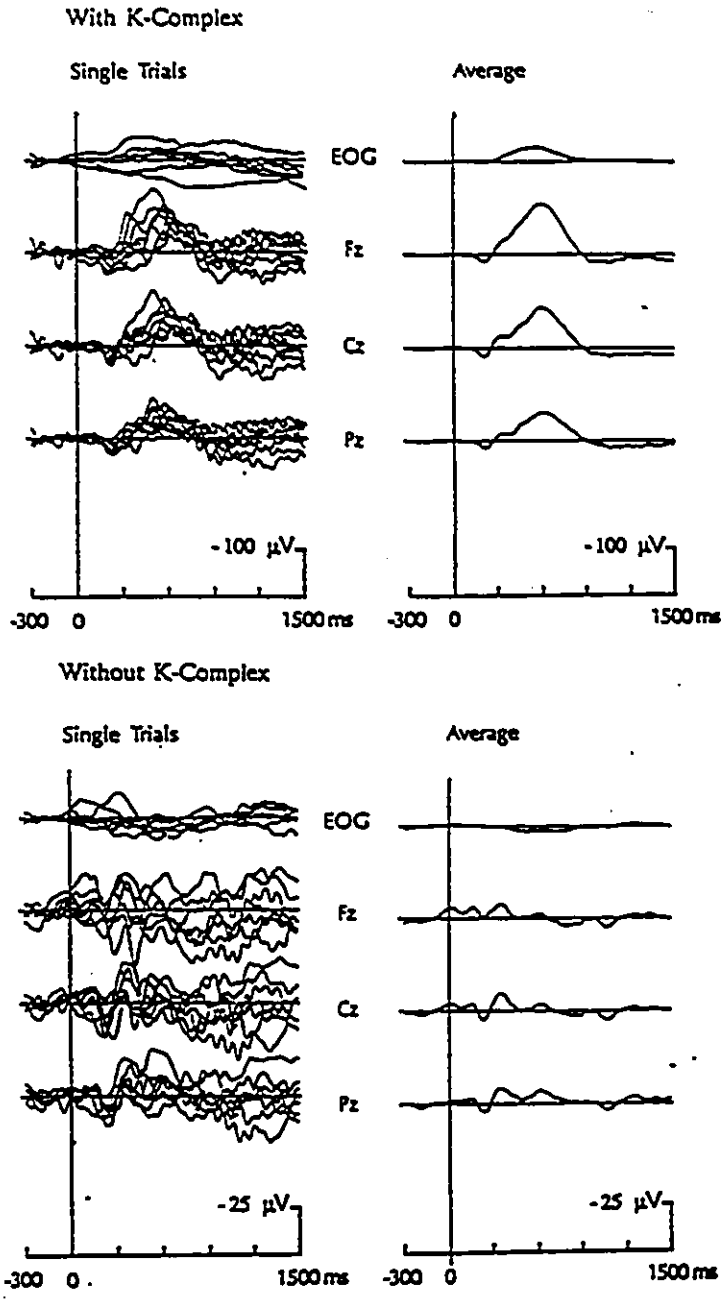
Figure Legends

Figure 1. Example of the averaging procedure used. Single trial K-Complexes for one subject are shown in the top portion while trials not containing a K-Complex are shown in the bottom portion. Single trials are shown in the left-hand column while the average of these single trials is shown in the right-hand column. As may be observed, the average is a good representation of the single trials, although there is considerable background noise that contributes to intra-trial variability.

Figure 2. Grand Averages of all subjects in all sleep stages for the 5, 10 and 30 sec ISI conditions. Note that the average of trials containing a K-Complex (left-hand side) is plotted at ¼ the amplitude of the average of trials not containing a K-Complex (right-hand side). Significant differences were found in the amplitude of N350 and N550 throughout the different ISI conditions, the two components being larger under the 30 sec ISI than under the 5 and 10 sec ISI. No significant differences were observed for P900 for the different ISI conditions. No significant differences in the amplitude of the various peaks were found between the 5 and 10 sec ISI conditions. No differences were found for N350 on trials in which no K-Complexes could be identified.

Figure 3. Procedure for selection of trials with 3 consecutive K-Complexes. In the first block of nine trials, a K-Complex is visible on the first, second and third trials; in the second block of nine trials, a K-Complex is visible on the fifth, sixth and seventh, while on the n^{th} block, a K-Complex is visible on trials 7, 8 and 9.

Figure 4. Grand Averages of all subjects in all sleep stages for the 5, 10 and 30 sec ISI conditions when 3 consecutive K-Complexes were identified. Results showed that while a significant attenuation in the amplitude of N350 and N550 in the Short ISI condition and a significant attenuation in the amplitude of N550 in the Medium ISI condition were observed, no significant decline in amplitude for any of the various peaks was found under the Long ISI condition.


With K-Complex
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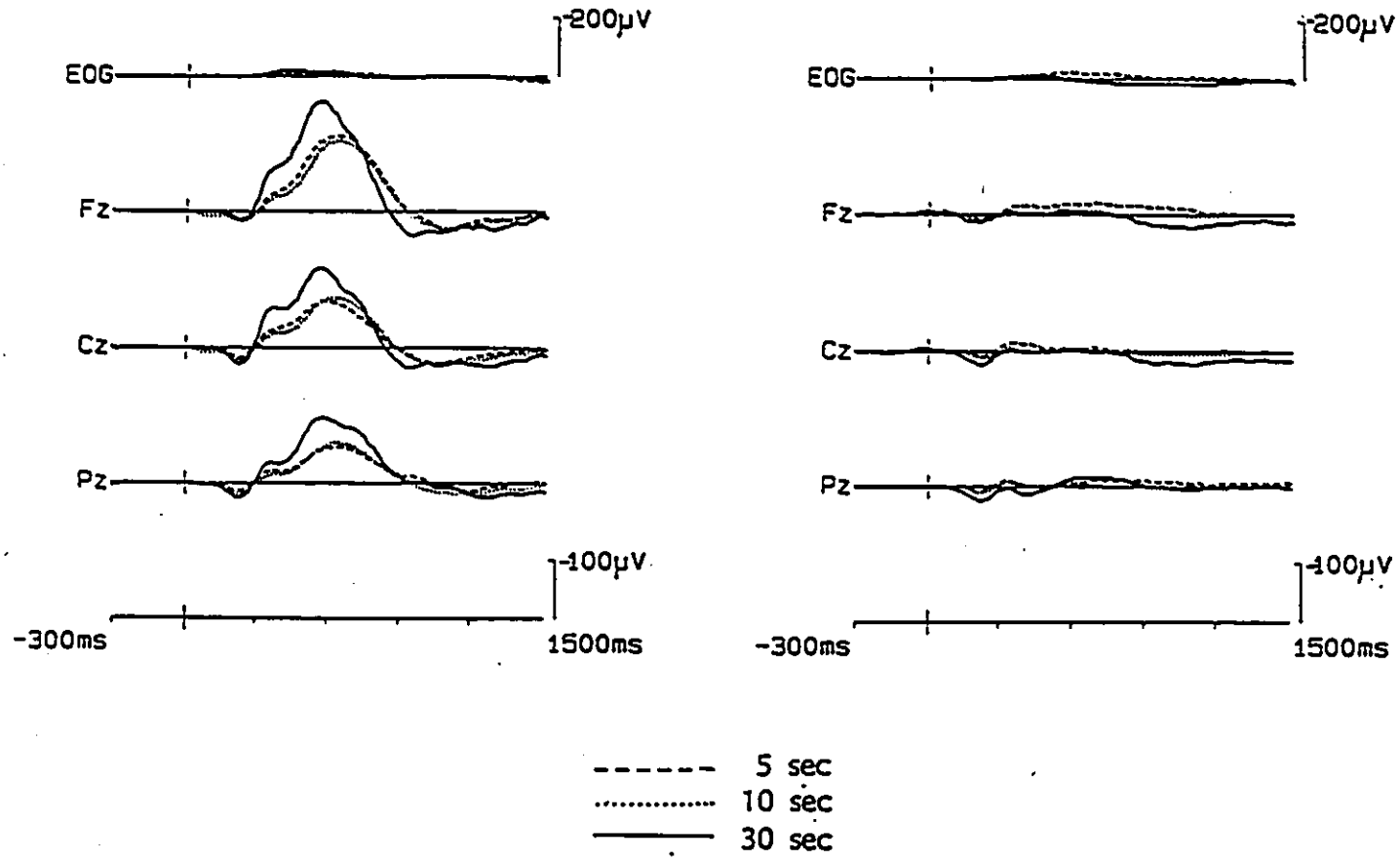
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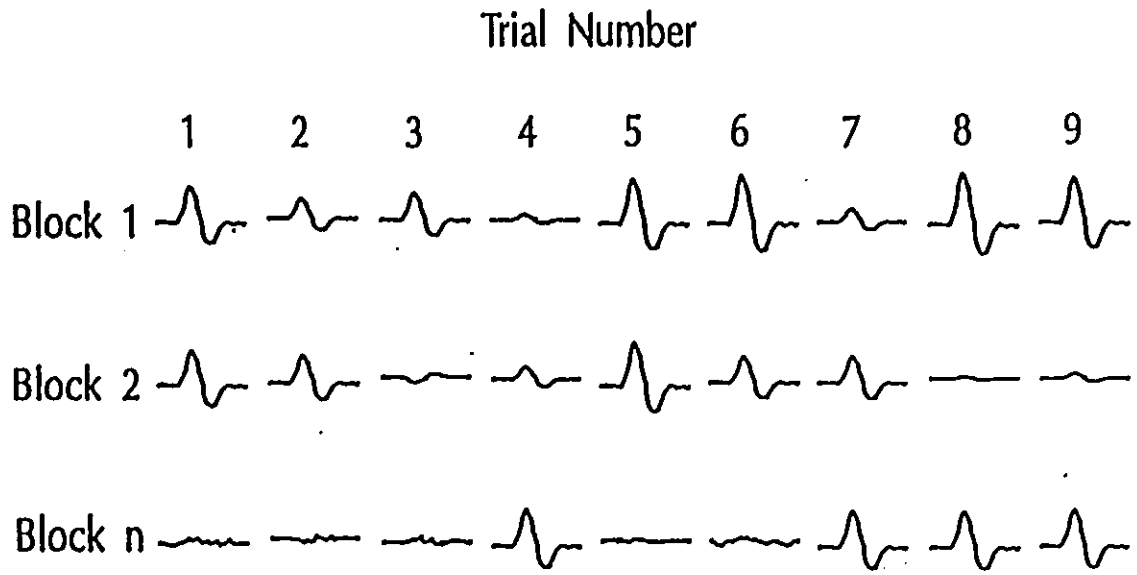
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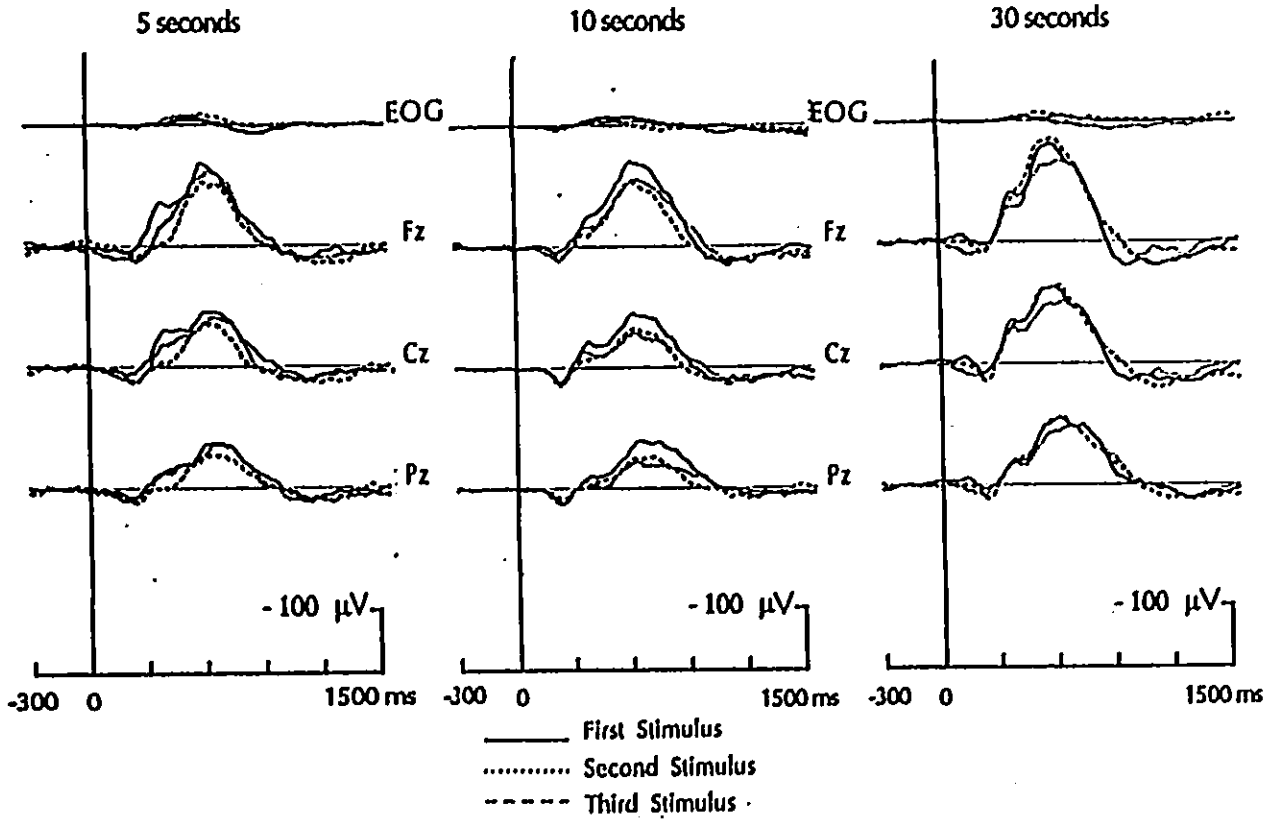
5 seconds
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Second Stimulus
Third Stimulus

Chapter 4

Experiment 3

Consequences of the evoked K-Complex.

Introduction

The previous chapters in this thesis have described the morphology of the K-Complex and the conditions under which it can be elicited. It consists of a large amplitude negative deflection ("N550") peaking between 500 and 600 msec followed by a positive wave ("P900") peaking between 800 and 1200 msec. The K-Complex appears as a phasic event occurring only in non-REM sleep. It is elicited most often by loud, abrupt stimuli that occur at slow rates of presentation. When a K-Complex is elicited, the amplitude of the N550-P900 complex does not vary significantly despite changes in stimulus parameters. When consecutive K-Complexes are elicited, there is a decrement in the amplitude of N550 upon repetition of the stimulus but only if the stimuli are presented faster than every 20 sec.

The third experiment was designed to study the consequential effects of the K-Complex. Two prominent and opposite theories have been offered to explain the functional role of the K-Complex. On one hand, some authors (Roth, Shaw and Green, 1956) have speculated that the K-Complex is an arousal mechanism. On the other hand, it has been suggested that the K-Complex is a mechanism that protects the sleeper against awakenings (Walter, 1963; Hess, 1965).

Evidence in support of either position has come from an analysis of the frequency and amplitude of the EEG prior to and following the K-Complex. A movement toward higher frequency and lower amplitude EEG is generally accepted to be indicative of a sign of higher arousal. By contrast, a movement toward lower frequency and higher amplitude is taken to be a sign of lower arousal.

Roth et al. (1956) provided data supporting the notion that the K-Complex was an arousal reaction. They used a visual inspection of the EEG and claimed that there was a tendency for the EEG to move toward higher frequency and/or spindle activity following the occurrence of a K-Complex. The function of the K-Complex was thus hypothesized to be a correlate of a "crude perceptual process which tended to initiate arousal". However, they did not carry out a statistical analysis of these observations. Moreover, they did not indicate the duration of the changes that they observed. Ehrhart, Ehrhart, Muzet, Shieber and Naitoh (1981) suggested that spontaneous K-Complexes appear to precede phases of transient activation (PATs or "Phases d'activation transitoire"). PATs are transient signs of arousal in which: a) the EEG increases in frequency and decreases in amplitude; b) alpha and other waking EEG patterns appear; and, c) body movements appear along with an increase in heart rate (Schieber, Muzet & Ferrière, 1971). Other studies have shown that when PATs are occurring, K-Complexes hold an antagonistic relationship with spindles. An increase in the number of K-

Complexes leads to a decrease in spindles which in turn, leads to a PAT (Antony-Baas, 1975; Naitoh, Antony-Baas, Muzet & Ehrhart, 1982). From these studies, it would thus appear that spindles serve as inhibitory mechanisms whereas K-Complexes are signs of arousal.

In contrast, Walter (1963) suggested that the K-Complex appeared to "...flatten the significance of intrusive signals..." (p.242). While the K-Complex is a response to stimuli, the information that is extracted is not so critical to cause the subject to fully awaken. The K-Complex thus drives the individual back to a deeper state of sleep. Hess (1965) thought that the N550-P900 component may play a significant role in the prevention of awakenings. Evidence to support the "drive into sleep" theory has been provided by Beier & Kubicki (1987). They noted the appearance of slow wave delta activity in the EEG following the K-Complex.

A problem with early studies is that the EEG was scored visually. Only the largest and most obvious changes in the EEG can be detected by the human eye. Frequency detection is notoriously unreliable. Recently, researchers have relied on computerized analyses of the EEG, typically involving Fast Fourier Transformations (FFTs) and/or spectral analyses. For instance, Pál, Simon and Halász (1985) noted that the occurrence of a K-Complex can be predicted from the power density function of a 1.8 sec EEG segment preceding the stimulus. They suggested that evoked K-Complexes are linked to a certain "brain state" (or

level of activation) prior to receiving stimulation. This brain state consists of "finely graded microstates" of arousal (short and fast power elevation toward higher frequency) that can be measured in stage 2 and possibly in stages 3-4.

Halász (1991) observed slight arousal shifts (i.e., microarousals) for 10-15 sec following presentation of a stimulus. The post-stimulus pattern was characterized by a short initial power elevation followed by a reduction of the delta, theta, alpha and beta frequency bands along with a gradual reduction of the 13-14 Hz sigma spindle band. Halász and Ujszászi (1991) used a more precise second-by-second FFT analysis of the post-stimulus period. Their results showed both a power elevation for the delta, theta, alpha and beta frequency bands and a power reduction for the sigma spindles. The return back to baseline values extended beyond the 10 sec analysis period. Power in the delta, theta, alpha and beta bands showed large increases in the first 2 sec, slowly decreasing back toward baseline values, while spindle power gradually decreased following the stimulus.

A problem with the Halász and Ujszászi (1991) studies is that their conclusions are based solely on trials on which a K-Complex was elicited by the stimulus. Changes in the EEG following the K-Complex could be due to the consequences of the K-Complex or to the stimulus itself. The authors failed to examine trials on which a K-Complex could not be elicited. Furthermore, the authors did not specify how they defined a K-

Complex. It is possible, for example, that isolated delta waves might have falsely been considered to be K-Complexes during NREM sleep.

It is apparent that previous attempts to determine the functions of the K-Complex are fraught with methodological difficulties. In the present study, the functional role of the K-Complex will be evaluated by spectral analyses of the EEG prior to and following the stimulus. Trials on which a K-Complex is elicited will be compared to trials on which it is not. The examination of trials on which no K-Complexes are identified will be made in order to determine the effects of the stimulus itself on the EEG power spectra. The EEG will be divided into four second time intervals prior to (two intervals) and following the onset (two intervals) of the stimulus.

Methods

Subjects

Ten adults (3 males, 7 females), between the ages of 18 and 34 years old ($\bar{X}$ = 24) were tested in a single all-night session. They were instructed to refrain from alcohol and drug use prior to the experiment. Prior to participating in the study, all subjects were asked to read a consent form that explained the experimental procedures. Each subject received an honorarium for their participation in the study.

EEG Recording

The EEG was recorded with Grass gold cup electrodes placed at midline frontal, central and parietal sites (Fz, Cz and Pz). The reference was the mastoid contralateral to the ear of stimulus presentation. The EOG was recorded with electrodes fixed at the supra-orbital ridge of one eye and the infra-orbital ridge of the other. This allowed the recording of horizontal and vertical eye movements on a single polygraphic channel. Inter-electrode impedance was maintained below 5 kOhms.

The high filter was set at 35 Hz and the time constant was 1 sec. The EEG was digitized at a rate of 128 Hz and stored continuously on hard disk over the entire night for later off-line analysis.

Procedure

Each subject was individually fitted with a hearing-aid/ear mould device through which the auditory stimuli were presented. The hearing-aid device assured a constancy of stimulus input despite the changes in head position during the night (Campbell & Bartoli, 1986).

K-Complexes were elicited by auditory stimuli. The stimuli were 80 dB SPL 2000 Hz tone pips having a total duration of 52 msec with a rise-and-fall time of 2 msec. The first study in this thesis demonstrated that stimuli having these characteristics had the highest probability of eliciting a K-Complex. Stimuli were presented in blocks of 15. Each stimulus

was presented at an inter-stimulus interval (ISI) of 20 sec. Time between blocks varied from 2 to 5 minutes. Stimuli were delivered during definite stage 2, 3 and 4 of sleep. Stage 2 was subdivided into early (2E) and late (2L) halves of the night to examine possible time-of-night effects. Stages 3 and 4 were combined to form Slow Wave Sleep (SWS). Stimulus presentation was halted and the data removed from further analysis when the EEG pattern showed signs of artifacts (e.g. body movement) or the onset of waking state. If raters disagreed (less than 5% of conditions), the condition was rejected from further analysis. Each block of 15 stimuli was repeated at least once in each stage of sleep to ensure replicability of the results. For most subjects, time allowed at least three repetitions of each block. One experienced rater later classified the stages of sleep according to the standard Rechtschaffen & Kales (1968) method. In the rare cases of stage classification ambiguity (again less than 5% of conditions), records were later scored by a second, experienced rater.

EEG Analysis

The single trials were sorted into those containing and not containing a K-Complex. A set of algorithms was employed for the definition of a K-Complex. Following stimulus presentation, the EEG sweep had to have a negative peak occurring between 400 and 650 msec followed by a positive peak occurring between 700 and 1200 msec. Their peak-to-peak amplitude had to exceed 75 μV.

Finally, the negative peak had to have a maximum frontal distribution. The pattern of the K-Complex was recognized by an automatic computer scoring routine following these above-mentioned criteria (Bell, Campbell, Deacon-Elliott & Noldy-Cullum, 1988). This method reduced the inclusion of random background noise as a K-Complex. These criteria were particularly required in SWS sleep where delta waves could be mistakenly identified as a K-Complex.

The EEG was divided into 4 sec segments relative to stimulus onset. Fast Fourier Transformations (FFTs) were computed for the following intervals: from 8.0 to 4.0, from 4.0 to 0.0 sec prior to stimulus onset and, from 1.25 to 5.25 sec and from 5.25 to 9.25 sec following stimulus onset. A 1.25 sec delay following stimulus onset was employed to avoid including portions of the K-Complex (having a duration of approximately 1 sec) in the FFT analysis. The FFTs were run at each electrode site. The resolution of the FFT was 0.25 Hz, the frequency range being from 0 to 20 Hz. Trials were sorted and analyzed separately from those on which a K-Complex was identified and those on which it was not identified.

The EEG was then broken down and "summarized" into a series of 5 frequency "bands" (range): delta (0.75-4.00 Hz), theta (4.00-8.00 Hz), alpha (8.00-12.00 Hz), sigma (12.00-14.00 Hz) and beta1 (14.00-20.00 Hz). The sigma band corresponded (but was not necessarily identical) to spindle activity. The logarithm of the "absolute" activity was obtained by the integration (or

computation of the area under the curve) of the power spectrum within each frequency band (i.e., the power was integrated first and the logarithm of the integrated power was then computed). The log of the power computation was considered necessary to compensate for the very large power of delta waves. The slow frequency, high amplitude delta waves would tend to "overwhelm" the lower amplitude, higher frequencies during sleep (and in particular NREM sleep). The relative activity for each frequency band was then computed by dividing their absolute values by the total band and was expressed in a percentage. Relative values are actually values of the ratio: log (r/(1-r)), where r is the relative power. Such a computation is in accordance with recommended EEG practise (Gasser, 1982).

Ratios of the high to low frequency bands were then computed. The first ratio was the quotient of the sum of delta and theta divided by the sum of alpha and beta1 [(delta+theta)/(alpha+beta1)] = SW1. The second ratio was the quotient of theta divided by alpha [(theta)/(alpha)] = SW2. The two ratios provide a convenient and often used summary of the proportion of lower to higher frequency activity. A higher ratio is reflective of lowered arousal.

Data analysis

FFTs and spectral analyses were computed prior to and following each of the fifteen stimulus presentations. The data were then collapsed across each of the trials on which a K-

Complex could be identified and the trials on which a K-Complex could not be identified. A general comparison (independent of stage of sleep) of the segments prior to and following stimulus onset or according to the presence or absence of a K-Complex could not be carried out because of the massive amount of all-night sleep data. The data were made more manageable by considering each stage of sleep separately. To determine the effects of stimulation on the log power of the different EEG bands, two-way repeated measures ANOVAs were therefore performed. An initial two-way ANOVA with repeated measures on K-Complex (present or absent) and scalp site (Fz, Cz, Pz) was run for each of the time intervals (8.0 to 4.0, 4.0 to 0.0 sec prior to stimulus onset and, 1.25 to 5.25, 5.25 to 9.25 sec following stimulus onset). A second two-way ANOVA was run to compare time intervals (8.0 to 4.0 vs 4.0 to 0.0 sec; 4.0 to 0.0 vs 1.25 to 5.25 sec; 1.25 to 5.25 vs 5.25 to 9.25 sec). A separate ANOVA was run when a K-Complex was elicited and another for when it was not. For each ANOVA, the dependent variables were: the absolute and relative activity of the delta, theta, alpha, spindle (sigma), beta1 bands, the total absolute activity, SW1 and, SW2.

Analyses were carried out using BMDP P2V procedures. For all comparisons, the significance level was set at $p<.05$. An assumption for use of repeated measures ANOVA is that of sphericity. This assumption was tested using the Wilk's Lambda procedure. When this assumption was violated, Greenhouse-Geisser correction procedures were applied.

Results

Across all conditions and stages of sleep, a K-Complex was elicited on approximately 50% of all trials. The number of elicited K-Complexes did not differ across the stages of sleep ($F < 1$).

Presence or absence of a K-Complex

Tables 1 and 2 summarize the influence of stage of sleep and the consequences of a K-Complex. The initial results will examine the power spectra of the EEG on trials on which a K-Complex was elicited and compare it to trials on which it was not elicited. No significant differences in the power spectra were found for any of the different scalp sites ($F<1$) and only frontal recordings are reported.

----------Insert Tables 1 and 2 about here ----------

Stage 2

In stage 2 (early and late), the presence or absence of a K-Complex had no effect on the EEG. Thus, the EEG spectrum prior to the presentation of the stimulus did not differ ($F<1$ in most cases) on trials on which a K-Complex was elicited compared to when it was not. Similarly, the EEG spectrum following the presentation of the stimulus did not differ ($F<1$ in most cases) on trials on which a K-Complex was elicited compared to when it was not.

SWS

During SWS, the EEG spectrum prior to the presentation of the stimulus did not significantly differ ($F<1$) on trials on which a K-Complex was elicited compared to when it was not. However, differences did emerge following stimulus presentation. For the post-stimulus intervals, the absolute log power of theta, alpha, sigma and beta1 activity was significantly higher following stimulus presentation on trials on which a K-Complex was not elicited compared to when it was [$F(1,8) = 6.50$, 3.76, 4.60 and, 4.06, respectively, $p<.05$].

Pre- and post-stimulus differences

The time interval immediately prior to the stimulus (i.e., 4.0 to 0.0 sec) and immediately following (i.e., 1.25 to 5.25 sec) were then compared. Tables 3 and 4 summarize the influence of stage of sleep and the consequences of a K-Complex. In the post-stimulus interval, the presence of a K-Complex did not have an effect ($F<1$) on the EEG spectra in any stage of sleep. In Stage 2 (either early or late), in the post-stimulus interval, the absence of a K-Complex did not have an effect ($F<1$) on the EEG spectra. On the other hand, during SWS, the post-stimulus time intervals on which a K-Complex was not elicited revealed a significant power elevation. During SWS, when no K-Complex was elicited, the log power of absolute theta, alpha, sigma and beta1 activity significantly increased following stimulus onset compared to prior to its onset, $F(1,8) = 4.17$, 9.56, 10.89 and,

5.21, $p<.05$. When a K-Complex was elicited, the EEG spectra did not significantly change from pre- to post-stimulus periods. Again, no significant differences in the power spectra were found for any of the different scalp sites ($F<1$) and only frontal recordings are reported.

---------- Insert Tables 3 and 4 about here ---------

First Stimulus

When a K-Complex was not elicited, analysis of post-stimulus intervals revealed that the log power of the absolute theta, alpha, sigma and, beta1 activity was significantly higher in the post-stimulus intervals compared to the pre-stimulus intervals. This observation was apparent in SWS. On trials in which a K-Complex was elicited, the EEG was not significantly different in the pre- and post-stimulus intervals.

Averaging procedures (data were collapsed across all trials) may have masked differences that occurred within single trials. It is possible, for example, that arousal/de-arousal changes might occur only on the first trial but not on subsequent trials. Collapsing across trials is thus not appropriate for the observation of an initial elevation or diminution in power in the different spectral bands. A separate analysis of the first trial was therefore carried out. This analysis has another advantage. There is a possible contamination in the pre-, post-stimulus analysis. The post-interval (12 to 20 sec) could be considered

to be the pre-interval for the subsequent stimulus. Only on the first trial is the pre-stimulus period not also a post-stimulus interval. FFTs of the pre- and post-stimulus intervals were compared for the first trial only. Again trials on which a K-Complex was and was not elicited were considered separately.

A K-complex was evoked on approximately 40% of all first trials for each train of stimuli. Although not significant ($F<1$), K-Complexes were elicited more often in stage 2E and 2L than in SWS on the first trial. When a K-Complex was elicited, there were no significant differences ($F<1$) in any bandwidth for any stimulus interval across all stages of sleep. No power elevation or diminution in any frequency bands, or any of the ratios was observed on the pre- and post-stimulus interval ($F<1$). Moreover, there was no interaction with scalp sites ($F<1$).

When no K-Complexes were elicited, as with the global analyses of all trials, again during SWS, the log power of absolute theta, alpha, spindle and beta1 activity significantly increased following stimulus onset compared to prior to its onset, $F(1,8) = 3.22, 7.46, 9.67$ and, 5.01, $p<.05$. There were no other significant differences.

Discussion

The functional significance of the K-Complex has long been a subject of theoretical debate. It has been considered to be a mechanism that elicits arousal in the sleeping subject (e.g. Halász, 1991; Halász, Pál and Rajna, 1985; Rajna, Halász, Kundra

and Pál, 1983; Roth et al., 1956) or a mechanism that prevents arousal (Beier and Kubicki, 1987; Hess, 1965; Walter, 1963). It was expected that if the K-Complex served as a mechanism to arouse the subject from sleep, the EEG following its occurrence would show movement toward higher frequencies. On the other hand, if the K-Complex served as a mechanism protecting the sleeping subject from awakening, it was expected that the EEG would show movement toward lower frequencies or remain unchanged following its elicitation.

On trials on which a K-Complex was not elicited, there was greater power in the higher frequency bands during SWS. The log power of the absolute theta, alpha, sigma and, beta1 activity was slightly, but significantly, higher in the post-stimulus intervals. No significant changes were observed for delta activity. The stimulus per se therefore appeared to elicit a small brief arousal in the sleeping subject. On trials on which a K-Complex was elicited, no changes in the EEG were noted following stimulus presentation. Thus the brief arousal that was apparent when a K-Complex could not be elicited was not apparent when a K-Complex could be elicited.

This therefore provides indirect support for theories that claim that the K-Complex serves as a mechanism protecting against awakenings. An auditory stimulus increases arousal from SWS. However, if it also elicits a K-Complex, it appears that this subsequent arousal does not occur. These latter findings, however, contradict the recent results obtained by Halász and

Ujszászi (1991). They observed a brief initial power elevation within 2 seconds of the stimulus, followed by a reduction of the delta, theta, alpha and beta frequency bands along with a gradual reduction of the 13-14 Hz sigma spindle band on trials on which a K-Complex was elicited. The difference between the results may be explained by the fact that Halász and Ujszászi (1991) did not isolate the effect of stimulation from the consequences of the evoked K-Complex. While spectral analyses were carried out on trials on which a K-Complex was elicited, they were not carried out on trials on which a K-complex was not elicited. They were thus unable to evaluate the impact of stimulation per se on the EEG. Hence, the microarousals observed by Halász (1991), Halász and Ujszászi (1991) could have been the consequences of stimulation itself and not a consequence of the evoked K-Complex.

Of course, this does not explain why they observed an elevation in power following the K-Complex while in the present study, we did not. Both studies used relatively loud (70 dB SL in the Halász and Ujszászi study is comparable to the 80 dB SPL in the present study) tone-pips (1200 versus 2000 Hz). The rise-and-fall time was much slower (20 msec in the Hungarian study) compared to the present abrupt 2 msec. Moreover, stimuli were presented with long and randomized ISIs (on average 30 sec) compared to 20 sec in the present study. As indicated in the second experiment of this thesis, ISIs longer than 10 sec appear to have minimal effect, at least on the likelihood of eliciting K-Complexes. Moreover, even when the spectral analyses were

carried out following the first stimulus, no changes were observed in the EEG when a K-complex was elicited. The time between the last stimulus presentation (in the previous block of trials) and the initial stimulus was at least *2 minutes*. The variation in the ISI between the two studies therefore appears to be a poor candidate to explain the discrepancies in the results.

The initial power increase observed by Halász and Ujszászi (1991) and Halász (1991) occurred within 2 sec of the stimulus onset. This could be due however to the frequency content of the K-Complex itself. The present study did not begin its analysis until 1.25 sec after stimulus onset.

In addition, their analyses were based on one sec "segments" within a 10-15 sec time interval (as opposed to 4 sec intervals used in the present study). It is possible that shorter time intervals are more sensitive to "microarousals". In Figure 3 of the Halász and Ujszászi (1991) article, it is apparent that in the 4 to 8 sec post-stimulus period, there is an initial augmentation in power (at least in the delta and the 17-22 Hz frequency bands) followed by a small decrease. The average of this 4 sec period (which would effectively sum the increase and the decrease) would therefore indicate no change in power. This would, of course, be in agreement with the present study. While other frequency bands showed a consistent decrease in power in the 4 to 8 sec period, the change was very small, averaging less than 0.01 μV^2 change in log power. The exception was the 13-14

Hz sigma (or spindle) band where "a striking deviation was found" (p.90).

Finally, many different types of K-Complexes in the Halász and Ujszászi's (1991) study were visually identified on single trials. The lack of precise definition of a K-Complex increased the probability of including random delta waves and background noise as a K-Complex. As mentioned earlier, the most "striking" effect that Halász and Ujszászi (1991) noted was in the spindle band. It is possible that their visual detection of K-Complexes was subject to a spindle bias.

It is possible that the K-Complex provides a means of extracting particularly relevant or highly salient information. Once the content of this information is extracted, further processing is inhibited. On the other hand, if the same identical stimuli do not elicit a K-Complex, a general arousal pattern of the EEG (perhaps reflecting higher cortical processing) will occur. The K-Complex may therefore serve to "gate" or attenuate processing of information that may be relevant but not so relevant as to cause the subject to move towards wakening.

The increase in power following stimulation on trials on which a K-Complex was not elicited was observed only in SWS (stage 3-4). This might be attributed to a "first night" effect since subjects spent only one single night in the laboratory. it is possible that adaptation to the stimulus could occur on subsequent nights. Pál et al. (1985) have demonstrated that

presenting stimuli during a one night session had no effect on the mean duration nor the percentages of sleep stages compared to the undisturbed baseline/nights. Therefore, the differences observed in SWS are not easily attributed to a "first night" effect.

Another possible explanation for the present findings might be the use of spectral analyses. Spectral power is influenced by both the frequency and the amplitude of the EEG. The interpretation of differences in power therefore can be ambiguous. In the present study, the increase in power could be due to an increase in frequency and/or an increase in amplitude. The former is an indication of increased arousal. The latter, however, is generally considered to be a decrease in arousal. We considered the increase in power of the various frequency bands to be a reflection of increased arousal. This was because the significant changes that were observed occurred for higher frequencies (from theta to beta). The only band that did not show this change was that generally considered to be indicative of deepening of sleep, the delta band. The fact that there was no change in delta power in the present study is thus contrary to what the decrease in arousal hypothesis would have predicted.

Analysis of the first stimulus revealed that no change in the EEG could be observed in any frequency bands on trials on which a K-Complex was elicited. It followed the same pattern as the overall analysis on trials on which a K-Complex was not elicited -- i.e., an elevation in higher frequency bands

following stimulus presentation. The impact of the first stimulus on the EEG is less marked than that might have been expected. Pre-post differences that were observed when the data were collapsed across trials could not be due to an apparent confound -- the interval following a stimulus could be considered to be also the interval prior to the subsequent stimulus. The post-stimulus EEG, thus had enough time (8 seconds) to return to baseline values. Thus, in the present study, the post-stimulus did not contaminate the subsequent pre-stimulus interval.

In conclusion, this study tends to support the notion that the K-Complex serves as a protector of sleep. Nevertheless, a change in the EEG toward lower frequencies was not apparent following the elicitation of a K-Complex. The EEG remained unchanged in post-stimulus trials on which a K-Complex was elicited. Rather, the conclusion is based on the fact that a general movement toward increased power was observed when a K-Complex was not elicited by the stimulus.

Table 1
Mean log power for the 1.25 to 5.25 sec interval for trials on which a K-Complex was elicited (indicated by "+") compared to trials on which it was not elicited (indicated by "-").

EEG ACTIVITY (log power)	Stage 2E		Stage SWS		Stage 2L	
	+	-	+	-	+	-
Delta	101.30	106.83	107.44	108.22	92.70	95.40
Theta	76.60	78.00	78.00	78.56*	73.10	73.90
Alpha	65.60	66.70	64.00	65.56*	64.40	63.90
Sigma	55.40	56.00	50.22	53.44*	55.90	56.50
Betal	49.10	51.00	47.00	48.89*	50.30	50.10
Total	102.50	103.40	108.00	109.22	95.50	97.50
(De + Th)/ (Al + Bel)	1.55	1.53	1.67	1.64	1.45	1.50
(Th)/(Al)	1.17	1.17	1.22	1.21	1.14	1.16

Note. Data are from frontal recordings. * p<.05

Table 2
Mean log power for the 5.25 to 9.25 sec interval for trials on which a K-Complex was elicited (indicated by "+") compared to trials on which it was not elicited (indicated by "-").

EEG ACTIVITY (log power)	Stage 2E		Stage SWS		Stage 2L	
	+	-	+	-	+	-
Delta	99.30	101.07	107.78	109.00	94.20	96.20
Theta	76.20	77.70	77.89	79.22*	73.00	75.10*
Alpha	65.50	66.20	64.11	65.89*	63.70	65.00*
Sigma	53.80	56.60	51.89	54.33*	55.90	56.70
Beta1	49.03	49.70	48.56	50.33*	50.40	51.30
Total	100.60	103.30	108.56	109.33	96.40	98.60
(De + Th)/ (Al + Be1)	1.53	1.55	1.66	1.63	1.48	1.48
(Th)/(Al)	1.17*	1.17	1.22	1.21	1.14	1.16

Note. Data are from frontal recordings. * p<.05

Table 3
Mean Log Power in Pre- (4.0 to 0.0 sec; identified as "Pre") and Post-stimulus (1.25 to 5.25 sec; identified as "Post") intervals on which a K-Complex has been identified.

EEG ACTIVITY (log power)	Stage 2E		Stage SWS		Stage 2L	
	Pre	Post	Pre	Post	Pre	Post
Delta	101.30	101.30	106.87	107.44	93.60	92.70
Theta	76.40	75.00	77.33	78.00	73.00	73.10
Alpha	65.00	65.60	65.00	64.00	65.00	64.40
Sigma	54.10	55.40	52.22	50.22	55.90	55.90
Beta1	49.60	49.10	47.22	47.00	50.20	50.30
Total	102.70	102.50	107.67	108.00	96.20	95.50
(De + Th)/ (Al + Be1)	1.55	1.55	1.65	1.67	1.45	1.45
(Th)/(Al)	1.18	1.17	1.19	1.22	1.13	1.14

Note. Data are from frontal recordings. * p<.05

Table 4
Mean Log Power in Pre- (4.0 to 0.0 sec; identified as "Pre") and Post-stimulus (1.25 to 5.25 sec; identified as "Post") intervals on which no K-Complex has been identified.

EEG ACTIVITY (log power)	Stage 2E		Stage SWS		Stage 2L	
	Pre	Post	Pre	Post	Pre	Post
Delta	101.50	101.80	108.22	108.22	95.20	95.40
Theta	77.90	78.00	78.33	78.56*	73.90	73.90
Alpha	66.60	66.70	64.67	65.56*	64.00	63.90
Sigma	55.80	56.00	52.44	53.45*	56.90	56.50
Beta1	51.00	51.00	47.78	48.87*	51.10	50.10
Total	103.20	103.40	108.89	109.22	97.30	97.50
(De + Th) / (Al + Be1)	1.53	1.53	1.67*	1.64	1.48	1.49
(Th) / (Al)	1.19	1.17	1.21	1.21	1.15	1.16

Note. Data are from frontal recordings. * p<.05

Chapter 5

General Discussion

The purpose of this thesis was to study the morphology, antecedent conditions and the consequences of the evoked K-Complex. The three different experiments attempted to resolve conflicts in the literature concerning the different components of the evoked K-Complex.

N350

A negative wave peaking at about 350 msec (thus "N350") was observed on trials when the later much larger N550-P900 complex was elicited, and remained apparent on trials when N550-P900 could not be identified. In Experiments 1 and 2, N350 varied in amplitude between 13 and 80 μV on trials on which the N550-P900 was elicited and between 7 and 25 μV on trials on which N550-P900 was not elicited. N350 is therefore not unique to the K-Complex. Whatever its role, it must be different than that of N550 and P900. In the first experiment, it was suggested that N350 acted as a trigger for the N550-P900 complex. N350 might need to reach a critical threshold amplitude before the N550-P900 complex can occur. This interpretation was based on the fact that the amplitude of N350 varied directly with stimulus intensity on trials on which N550-P900 could not be elicited. N350 reached a "ceiling" maximum amplitude when N550-P900 was also elicited. This amplitude did not vary with further manipulation of stimulus

intensity. The K-Complex occurred more often following high than low intensity stimuli. This may be because the amplitude of N350 tended to be larger on trials on which the high intensity stimulus was presented. N350 reached its critical threshold more often, thus resulting in more frequent occurrences of N550-P900. This does not explain why, on certain trials when stimulus intensity was high, a K-Complex could not be elicited. Similarly, it does not explain why the K-Complex might be elicited on certain trials on which the stimulus intensity was low.

In the second experiment, the N550-P900 complex occurred more often when the rate of presentation was slow compared to when it was fast. Unlike the case in Experiment 1, N350 did vary in amplitude when N550-P900 was elicited. N350 was larger when the rate of stimulus presentation was slow. However, also unlike the case for Experiment 1, N550 also varied in amplitude -- it was larger when the rate of stimulus presentation was slow. When the N550-P900 complex is elicited, variation in its amplitude is paralleled by N350. This could be because N350 is overlapped in time and space by the N550-P900 complex. N550 increases in amplitude might therefore "pull up" N350, although the N350 process is not itself affected.

On trials on which the N550-P900 complex was not elicited, N350 did not vary in amplitude despite wide variation in the rate of stimulus presentation. This finding appears to be in contradiction to the interpretation offered for the findings in

the first experiment. N350 was larger in conditions where the K-Complex occurred more often. In the second experiment, K-Complexes occurred more often when the ISI was longer. If N350 is a trigger for the N550-P900, it (N350) should be largest in conditions in which N550-P900 occurs most often (i.e., when the ISI was long). This was not the case. The "trigger" hypothesis can still be accommodated if it is assumed that the refractory period for the N350 deflection is quite short, indeed shorter than the minimum 5 sec ISI used the present study. The refractory period for N550 was estimated to be between 10 and 30 seconds. The refractory period for N350 might be considerably shorter.

Roth et al. (1956) reported that with a rate of presentation shorter than 1 sec there was a suppression of responding (occurrence of a K-Complex). However, if the ISI was between 1 and 3 sec, intermittent responding was observed. Negative waves in the 300 and 400 msec latency range have been reported to occur with quite rapid rates of presentation. Picton and Hillyard (1988) observed what they called the "sleep N2" with an ISI of 1.1 sec. Similarly, Noldy et al. (1988) also observed an "N2" (latency 346 msec) at sleep onset (defined as stage 2) with an ISI of 1.1 sec. Hull et al. (1993) reported that the amplitude of a N350 wave was larger with ISIs ranging between 1.5 sec and 4.5 sec. With ISIs shorter than 1.5 sec and longer than 4.5 sec, the amplitude of N350 did not change. They thus seemed to have observed what could be called an "asymptotic amplitude plateau"

for N350. The refractory period of this component thus appears to be between 1 and 4.5 sec.

Hull et al. (1993) have indicated that N350 is also sensitive to the probability of stimulus presentation. In this study, a frequently occurring "standard" stimulus was presented. On certain rare trials, the tonal frequency of the standard stimulus was changed. This rarely occurring stimulus is called the "deviant". In the transition from waking to sleep, N350 is larger to the infrequent deviant stimulus than the standard (Hull et al., 1993). N350 might therefore act as a memory comparison mechanism. Frequently occurring stimuli will require less processing since the memory for such stimuli is well-formed. On the other hand, the memory for the infrequent, deviant stimulus is poor. Additional processing is therefore required.

Ujszászi and Halász (1988) proposed that N350 might be a better reflection of information processing than N550. This is consistent with our interpretation of the information processing role of N350. The amplitude of N350 might provide an index of the amount of processing that a stimulus receives. Results of Experiment 3 indicated that on trials on which the large N550-P900 complex is not elicited, the EEG showed signs of increased power following stimulus presentation. This increased power was observed for higher EEG frequencies. This is generally accepted to be indicative of increased arousal. The increased arousal might be a consequence of additional information processing. Ironically, the appearance of N350 (or the "sleep N2") has been

suggested to be a marker of sleep onset (Noldy et al., 1988; Ogilvie et al., 1991). This may be because N350, in its information processing role, interrupts sleep. If N350 is an arousal response, it might be expected that it should cause a movement towards the waking state. The information extracted is sufficient to cause a small but brief micro-arousal. When the K-Complex is not elicited (thus when only N350 is apparent), information processing, and hence cortical arousal, still occurs. Presumably, the amount of information extracted is sufficient to not disturb sleep and cause awakening. However, when N350 is larger in amplitude and reaches its critical threshold, it might be expected that sleep would be interrupted. This does not occur because the N550-P900 is elicited, driving the subject back to sleep. The role of the large N550-P900 may therefore be to prevent wakefulness. We hypothesize that N550 is elicited to prevent sleep disturbance by preventing the arousal typically seen following stimulus presentation.

Experiments 1 and 2 indicated that on trials on which the large N550-P900 complex was elicited, the N350 component was prominently distributed at the vertex. This central distribution of N350 was also reliably observed on trials on which the later N550-P900 complex was not elicited. These results are in agreement with Ujszászi and Halász (1988) who reported that their "N300" (N350 in the present study) had a maximal amplitude at the vertex. Ujszsaszi and Halász (1988) also reported that N550 and P900 were frontally and fronto-centrally distributed,

respectively, thus differing with N350 which was more central. Again, our results are in agreement with theirs, a similar distribution for N550 (frontal) and P900 (fronto-central) being observed in the present experiments.

N350 waves may not be apparent on trials on which a K-Complex is elicited if only frontal sites are examined. It is sometimes overlapped by the N550 wave, giving the appearance of a smooth, long-lasting slow wave. Nevertheless, an examination of central and parietal waveforms reveals a clear earlier N350 and a later N550.

N550

A negative wave peaking at about 550 msec (thus "N550") was observed on trials when a K-Complex was elicited. Unlike N350, N550 was not apparent on trials on which a K-Complex was not elicited by the evoking stimulus. N550 varied in amplitude between 55 and 200 μV on trials on which a K-Complex was elicited. N550 was consistently distributed frontally in both Experiments 1 and 2, across all stimulus conditions. As mentioned, these results are in agreement with previous reports (Ujszászi and Halász, 1988; Paiva and Rosa, 1991).

The N550-P900 complex was elicited more often following loud (high intensity) and abrupt (fast rise-time) stimuli. The N550 component of the averaged evoked K-Complex was not affected by manipulations in stimulus parameters. Its latency and amplitude remained invariant with different intensities (60 and 80 dB),

tonal frequencies (500, 1000 and 2000 Hz) and rise-and-fall times (2 and 20 msec). N550 thus seems to act as an all-or-none phenomenon. It is either elicited or not elicited. When it is elicited, its morphology is invariant in spite of differences in the physical qualities of the stimulus. These results are in agreement with the much earlier results obtained by Roth et al. (1956).

It could be argued that inter-trial variation of the N350-N550-P900 complex is lost through the averaging procedure. Averaging can distort the true single trial response if there is considerable variation in the peak latency of the components of interest. Such "latency jitter" will tend to attenuate or "smear" peak amplitudes. The averaging technique may not provide a good opportunity to look at a continuum of responses. Indeed, Halász et al. (1985) have postulated that individual K-Complexes might be graded and distributed along a continuum, especially in the transition from stage 2 to SWS. However, the extent to which trial-to-trial variation is due to true differences in the amplitude of the K-Complex or to the random overlapping summation of high amplitude background noise remains unclear. It is possible that recent single trial "averaging" techniques such as Woody filtering, could be applied to the K-Complex to compensate for possible latency jitter.

The fact that N550 is elicited by loud and abrupt stimuli suggests it may be a Defensive Response (DR) rather than an Orienting Response (OR). In support of this claim, previous

studies have indicated that heart-rate accelerates following either a spontaneous or an elicited K-Complex (Church et al., 1978; Johnson and Karpan, 1968). Heart-rate acceleration is a component of a DR (Graham, 1979).

In Experiment 2, N550 was observed to be attenuated with fast rates of stimulus presentation. This is not necessarily in contradiction with the all-or-none phenomenon functioning of N550. The attenuation was interpreted as being due to the fact that with relatively short ISIs (less than 10 sec), the stimuli are presented during the refractory period of N550. Its refractory period was estimated to be between 10 and 30 sec. Furthermore, when consecutive K-Complexes were elicited on different trials, N550 amplitude was larger following the initial than on subsequent presentations, at least for the 5 and 10 sec ISIs. With slower rates of presentation, the amplitude of N550 did not vary when consecutive K-Complexes were elicited. The attenuation of N550 upon repetition of the stimulus might be because of the habituation process. As such, N550 might be thought of as an OR. ORs are subject to habituation while DRs are not. It is possible to interpret the attenuation upon repetition of the stimulus in another manner. The fact that consecutively occurring N550s were attenuated only with relatively fast rates of presentation could also be interpreted as due to the refractory process.

The results of the third experiment also question the notion that N550 is an OR. A consequence of an OR is cortical arousal

(Sokolov, 1960), often in the form of alpha blocking in the awake subject. There was, however, no change in the power spectrum of the EEG following the occurrence of the N550-P900 complex. As mentioned previously, when N550-P900 could not be elicited, the EEG showed a small, but statistically significant increase in power across most of the frequency bands except for delta. Thus, while there are signs of increased arousal following stimulus presentation in the sleeping subject, when the stimulus also elicits the large N550-P900 complex, there is no evidence of arousal.

N550 could also be considered to be a precursor to the DR. DRs, being elicited by very loud and abrupt stimuli, might be expected to awaken the subject. In the present study, the intensity of the loudest stimulus (80 dB SPL) was well below the level considered necessary to elicit a DR in the awake and alert subject. The N550 process might have been sufficient to prevent movement to wakefulness for stimuli of this intensity.

A K-Complex cannot be elicited in stage REM. It is difficult to awaken a subject from REM sleep (Rechtschaffen and Kales, 1968). Mechanisms other than the N550 might therefore serve this protective role. Presumably, these mechanisms do not function in NREM sleep.

P900

A positive wave peaking at about 900 msec (thus "P900") was observed on trials on which a K-Complex was elicited and, to a

lesser extent, on trials on which it was not elicited. P900 varied in amplitude from 13 to 75 μV on trials on which a K-Complex was elicited. Only a small P900 (less than 10 μV) was apparent on trials when a K-Complex was not elicited. P900 took on the appearance of a long-lasting slow wave rather than a distinctive peak, such as N350 and N550. The extent to which this slow wave appearance is due to latency jitter could not be determined by the present experiments.

The results of the Experiments 1 and 2 revealed that P900 was fronto-centrally distributed. These results are in agreement with previous reports (Halász et al., 1985; Ujszászi and Halász, 1988).

Few researchers have suggested a specific role for P900. Graham and Clifton (1966) speculated it might serve as an index of attention and/or memory, although they had little data to support this claim. P900 does appear to be independent of N550. Its scalp topography, and hence its intracranial generators, are different. Experimental manipulations also affected P900 and N550 differently.

Like N550, the P900 component of the averaged evoked K-Complex was not affected by manipulations of stimulus parameters. Its latency and amplitude remained invariant with different intensities (60 and 80 dB), tonal frequencies (500, 1000 and 2000 Hz) and rise-and-fall times (2 and 20 msec). On the other hand, in both Experiments 1 and 2 on trials on which N550 could not be elicited, P900 was present (although much attenuated). Both N550

and P900 were affected by the rate of presentation, being larger with the 30 sec ISI than with the 5 and 10 sec ISI. On consecutive occurrences of the K-Complex, unlike N550, P900 amplitude was not altered by rate of presentation.

The interpretation of the P900 slow wave remains difficult. Slow waves following the endogenous P3 component of the event-related-potential in the awake subject have been postulated to reflect processes involved in closure, such as assessing the meaning of the completed trial and/or preparation for the next trial (Ruchkin et al., 1990). It is also possible that there may be several late positive peaks that through the averaging process appear as a single slow wave. Johnson and Donchin (1985) have demonstrated that a single task-relevant stimulus can elicit several late positive ("P3") waves. The average of these multiple P3s will form a slow wave.

Conclusions

Several original findings were reported in this thesis. They include:

1. The K-Complex consists of a series of components, that were labelled N350, N550 and P900. These are differentiated on the basis of their scalp topography and effects of experimental manipulations.
2. N350, N550 and P900 have different scalp topographies being centrally, frontally and fronto-centrally distributed, respectively. Their sites of intra-cranial generation must therefore be different.
3. The K-Complex occurs more often to loud and abrupt stimuli.
4. When the K-Complex is elicited, the N350-N550-P900 wave is not affected by manipulation of the physical parameters of the stimulus.
5. N350 (and to a lesser extent P900) is still present, although attenuated, when N550 cannot be elicited.
6. When N550 cannot be elicited, N350 varies in amplitude with the intensity of the stimulus.
7. The K-Complex occurs more often with slow (30 sec) than with fast rates of presentation (5 or 10 sec).
8. The refractory period for N350 appears to be quite short (less than 5 sec), while that for N550 is much longer (between 10 and 30 sec).

9. When N550 cannot be elicited, a slight micro-arousal can be detected following stimulus presentation. When N550 is elicited, no change in the EEG could be observed. N550 might therefore serve to prevent such micro-arousals from occurring.

10. The amplitude of N350 might reflect the extent of information processing. Once it reaches a critical amplitude threshold N550 is then, and only then, elicited.

Conclusions

Quelques résultats originaux furent rapportés dans cette dissertation. Ils comprennent:

1. Le Complexe-K consiste en une série de composantes qui furent nommées N350, N550 et P900. Elles furent différenciées selon leur distribution topographique et les effets des manipulations expérimentales.
2. N350, N550 et P900 ont respectivement une distribution topographique différente soit centrale, frontale et fronto-centrale. Leur site de génération intracrannien doit donc être différent pour chacune des composantes.
3. Le Complexe-K apparaît plus souvent avec des stimuli d'intensité élevée (80 dB) et de temps de montée rapide (2 msec).
4. Quand un Complexe-K est évoqué, le complexe N350-N550-P900 n'est pas affecté par la manipulation des paramètres physiques du stimulus.
5. N350 (et à une étendue moindre, P900) est toujours présent, même si atténué, lorsque N550 n'est pas évoqué.
6. Quand N550 ne peut être évoqué, N350 varie en amplitude avec l'intensité du stimulus.
7. Le Complexe-K apparaît plus fréquemment avec un IIS lent (30 sec) comparativement à un IIS rapide (5 ou 10 sec).

8. La période réfractaire de N350 apparaît être très courte (moins de 5 sec) tandis qu'elle semble plus longue pour N550 (entre 10 et 30 sec).
9. Quand N550 ne peut être évoqué, un micro-éveil minime peut être détecté après la présentation du stimulus. Quand N550 est évoqué, aucun changement ne peut être observé dans le EEG. N550 peut donc servir à prévenir d'éventuels micro-éveils qui pourraient survenir.
10. L'amplitude de N350 peut refléter l'étendue du traitement de l'information. Lorsqu'il atteint un seuil d'amplitude critique, N550 est à ce moment, et seulement à ce moment, évoqué.

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