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The effect of air travel on sleep and seizure frequency for individuals with epilepsy

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THE EFFECT OF AIR TRAVEL ON SLEEP AND SEIZURE FREQUENCY FOR INDIVIDUALS WITH EPILEPSY

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ABSTRACT

This study is an empirical investigation of a clinical observation that air travel, particularly extended east-west flight, promotes an increase in seizures for individuals with epilepsy. Literature on sleep, sleep loss, circadian rhythm disruption and transmeridian desynchronosis is reviewed to consider how these flight-related factors may lower seizure threshold. It was hypothesized that seizures would be more prevalent after air travel and that circadian rhythm disruption, sleep loss, sleep variability, and baseline seizure frequency would be related to an increase in post-flight seizure frequency. Thirty-seven individuals with epilepsy self-monitored their sleep and seizure frequency for one week prior to and one week after flying. Most individuals did not experience seizures during their involvement with the study. Of the 14 subjects that reported seizures, nine experienced an increase in seizure frequency, two experienced no change, and three experienced a decrease in post-flight seizures. Seizures were significantly more frequent during the post-flight week. Subjects reported sleeping less on the night before flying and during the night of air travel. However, sleep measures were not significantly associated with an increase in seizures after flying. Subjects who experienced an increase in seizures after flying flew farther than those who did not have an increase in seizures. Subjects with higher rates of baseline seizures were most likely to experience an increase in seizures after flying. This study suggests that air travel can promote seizures, particularly when the flight is extended and when the individual with epilepsy has poor control over his or her seizures. The theoretical and clinical implications of these results are discussed.

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INTRODUCTION

Epilepsy is characterized by recurrent seizures and is popularly considered the result of brain damage or of pathological brain physiology (Fenwick, 1990). Most epilepsy research has focused on brain mechanisms and the many factors influencing central nervous system functioning. Considerable attention has been spent in the pursuit of pharmacological methods of reducing seizures (for a review see Glaser, Penry, & Woodbury, 1989). While pharmacological therapies are the most prevalent and effective treatments known for epilepsy (Mattson, Cramer, Collins, et al. 1985; Spunt, Hermann, & Rousseau, 1986), there is now no known cure for epilepsy and anticonvulsant medications are not effective for all individuals with the disorder. Fewer than 50% of adults with partial or secondary generalized seizures remain free of seizures for more than 12 months (Mattson et al. 1985; Elwes, Johnson, Shorvon, & Reynolds, 1984). Anticonvulsants have frequent side effects, such as sedation, impaired learning and cognitive functioning, visual disturbances, and dermatitis (Niedermeyer, 1990; Penry & Rachel, 1986). Pharmacological treatment is difficult or inappropriate for patients with kidney or liver disease, for the elderly, and for the pregnant (Dalessio, 1985; Scheuer, 1991). When seizures fail to respond to antiepileptic drugs surgery is commonly considered the only alternative (Andermann, 1987; Gumnit, 1987).

The most common treatments for seizure disorders are pharmacological and surgical. These approaches are consistent with the medical model of seizure production, that is, that seizures are the result of dysfunctional brain physiology. The limits of pharmacotherapy, and the inherent risk of surgery, make it important to consider broader models of seizure genesis, and additional means of seizure management.

More inclusive models of seizure development have been proposed (e.g., Fenwick, 1991; Lockard, 1980) that posit that factors additional to physiological state contribute to seizure development. Environmental factors (for example, Forster, 1969; Neill & Alvarez,

1989), emotional factors (for example, Feldman & Paul, 1976), and cognitive–behavioral factors (for example, Zlutnick, Mayville, & Moffat, 1975) have been shown to contribute to seizure production. Treatments based on more inclusive models of seizure production have proven effective in reducing seizures. Behavioral methods, employing reinforcement, punishment, self-management, and desensitization techniques have proven effective (for example, Dahl, Melin, Brorson, & Schollin, 1985; Forster, 1972; Zlutnick et al., 1975). Psychophysiologically based treatments have also shown promise (for example, Birbaumer, Lutzenberger, Elbert, & Trevorrow, 1992; Sterman, 1973). Appreciating and reducing environmental, cognitive, and behavioral contributions to seizure production is critical in the management of many individuals' epilepsy. Aird (1988) found in a group of 150 refractory epileptic children that reducing the influence of seizure inducing mechanisms, such as alterations in sleep-wake cycle, fatigue, sleep deprivation and psychological stress resulted in a 50% reduction of seizures in 20% of the children, and complete control for 14% of the children. Some individuals can only reduce their seizures through cognitive, behavioral, and environmental strategies (Dahl, Melin, & Lund, 1987).

Among potential environmental variables, little is known about the impact of air travel on individuals with epilepsy. Air travel can present multiple psychological and physiological stressors to the general public and may be particularly challenging for an individual with epilepsy. For other than short commuter flights, air travel involves a disruption of mealtimes, work, recreation, and sleep schedules. For extended East or West flights, air travel also requires the traveler to adjust to a new time zone with all the accompanying disruptions of the traveler's circadian rhythms. Individuals with epilepsy may fear having a seizure in flight, or being in unfamiliar surroundings where medical resources are unfamiliar or inadequate (Travel Commission of the International Bureau for Epilepsy, 1973).

It remains to be established whether air travel is associated with seizure increases for individuals with epilepsy. Neurologists have clinically observed an association between

extended air travel and an increase in seizure frequency (J. W. Pearce, personal communication, April 18, 1990). Empirically establishing an association (or lack of an association), between extended air travel and seizure frequency may contribute to managing individuals with epilepsy who desire to travel by air. For example, if it is established that East-West circadian rhythm disruption is related to seizure increase, then breaking up a long flight into two or more shorter flights, with layovers, may reduce the likelihood of an increase in seizures. Similarly, if sleep disruption is associated with post-flight seizure increase, then interventions that promote regular sleep may be effective in reducing post-flight seizures. Determining what patient and environmental variables contribute to seizure increase may also help in establishing empirically based policies for air travel. The airline industry has no empirically based policies to determine if special precautions are necessary to assist passengers with epilepsy who travel by air. Yet, airlines have placed restrictions on passengers as a consequence of their having epilepsy (M. Cooper, personal communication, October 15, 1991).

This study investigated the impact of air travel on sleep and seizure frequency for individuals with epilepsy. The following is a review of basic definitions, classifications, and epidemiological data about epilepsy as well as a review of the literature on environmental, behavioral, and physiological factors associated with air travel that may influence sleep and seizure frequency.

What is Epilepsy?

Epilepsy is a recurrent paroxysmal disorder of cerebral function characterized by sudden brief attacks of altered consciousness, motor activity, sensory phenomena, or inappropriate behavior caused by abnormal excessive discharge of cerebral neurons (Labar, 1992). Epilepsy manifests in nearly two dozen different types of seizure disorders. Porter (1984), lists five methods of epilepsy classification: by seizure type and EEG, by etiology, by seizure magnitude, by seizure severity and chronicity, and by the body part influenced

by the seizure. Most often epilepsy is described using the etiologic classification and the description of the seizure expression (Porter, 1984).

Seizures are basically divided into 2 groups—partial and generalized. Partial seizures have clinical or EEG evidence that arise in a portion of one hemisphere, but the term "partial" does not imply a highly discrete focus—such a focus often does not exist. The local discharge may spread to the rest of the brain during a seizure. Generalized seizures, however, have no evidence of localized onset—the clinical manifestations and abnormal electrical discharge give no clue to the locus of onset of the abnormality, if indeed such a locus exists (Porter, 1984).

Partial seizures can be simple (with no loss of consciousness), or complex (with a loss of consciousness). A partial seizure may be preceded by an aura (a sensory experience that signals the development of a seizure). It is possible that a partial seizure may progress to a generalized seizure.

Generalized seizures are even more heterogeneous than partial seizures; they can be tonic (muscle contractions), clonic (muscle jerking), atonic (loss of muscle tone), "absence" (automatisms and unresponsiveness for several seconds), and infantile spasms. Most patients have stereotyped seizure patterns. Even when a patient reports a wide variety of seizure types, careful historical analysis will allow clustering of the seizures into 2 or 3 types (Porter, 1984).

Epilepsy Prevalence and Incidence

Hauser & Hesdorffer (1990) report the prevalence of epilepsy as 6.42 per 1,000; over two million persons with epilepsy in the U.S.A. The Epilepsy Foundation of America estimates over 1% of the population have epilepsy (Graybeal, 1991). Prevalence is typically much higher for children than for adults: about 50% of epileptics are under 18 years of age. There are approximately 125,000 new cases of epilepsy in the U.S. each year (Hauser & Hesdorffer, 1990). The probability that any healthy individual will develop

epilepsy during his or her lifetime is estimated between 1.3 and 3.1 percent (Hauser & Hesdorffer, 1990).

Individuals with Epilepsy Who Fly

Air travel has become increasingly accessible. Four hundred and fifty three million passengers enplaned in the US. in 1989—a rate over two and a half times as many as enplaned in 1970. Thirty-one million flew between the United States and foreign countries in 1989; 9.8 billion passenger-miles were traveled by domestic air travel (US. Bureau of the Census, 1991).

There are no published estimates of the number of individuals with epilepsy who travel by air. Estimates using the national prevalence rate of epilepsy are likely to be too high, considering the low income of many individuals with epilepsy (Whitman, Coleman, Berg, King, & Desai, 1980). There may also be a reluctance of some individuals with epilepsy to travel, due to anticipated difficulties with undertaking such travel (Travel Commission of the International Bureau for Epilepsy, 1973). A calculation using one-tenth of the estimated prevalence rate for epilepsy (i.e., .001 of the US population) results in a conservative estimation of approximately 450,000 individuals with epilepsy who enplaned in 1989. Air travel has the potential of effecting hundreds of thousands of epileptics each year.

Epilepsy & Sleep

If air travel lowers seizure threshold, it likely to do so through disrupting sleep. Air travel, particularly extended east-west flight, typically causes sleep disruption and sleep loss (Nicholson, 1972). Sleep disruption and sleep loss in turn have been associated with the promotion of seizures for individuals with epilepsy (Jovanovic, 1967). The following three sections have been devoted to various aspects of the relationship of sleep to epilepsy.

History

Epileptic seizure distribution has been linked to the sleep-wake cycle for over 2,000 years (Broughton, 1978). Systematic studies of the occurrence of seizures during sleep have been conducted from the later half of the 19th. century (Fere, 1890; Gowers, 1885); studies spanning the past century reveal that clinical manifestations of virtually all seizure disorders are in some way related to sleep (Shouse, 1986).

The sleep-wake cycle formed the basis of early seizure classification schemes. For example, Gowers (1885) differentiated patients who had seizures either mostly at night, mostly during the day, or randomly throughout the day and night. Today, authors maintain that most epileptics have seizures entrained to the sleep-wake cycle (Shouse, 1986).

That sleep is related to increased seizure occurrence was also documented in early clinical observations. Fere (1890) established, in a three month study of in-patient epileptics, that two-thirds of the seizures occurred during sleep. Gowers (1885) observed that the most frequent times for seizures to occur were at the onset, and at the end of sleep. This observation has been reported for over a century (for example, Janz, 1962; Langdon-Down & Brain, 1929; Patry, 1931; Shouse, 1986). Most contemporary authors agree on these peak times for seizure occurrence in waking and sleep epilepsy (Shouse, 1986).

Sleep Architecture

Advances in psychophysiological methods, primarily the development and use of EEG, have led to an increased understanding of sleep architecture and how sleep may interact with the epileptic brain. Before the 1930s, sleep was considered to be simple, passive, and

uniform (Hauri, 1982). However, with the advent of the EEG, sleep was found to have several distinct electrophysiological patterns (Loomis et al., 1937) that can be classified into stages: rapid eye movement (REM) and non-rapid eye movement (NREM) (Aserinsky & Kleitman, 1953). NREM sleep was further recognized as having four stages that reflect the depth of sleep. REM and NREM stages progress in a more or less consistent ultradian cycle that repeats about every 90 minutes for adults, and every 60 minutes for infants (Hauri, 1982).

Upon going to bed, adults typically fall into a state of relaxed wakefulness, characterized by 8 to 12 cycles per second (Hz) called alpha waves. Sleep onset occurs when the individual goes through stage 1 (3 to 7 Hz theta waves) and pass into stage 2 characterized by 12 to 14 Hz waves. Most adults enter deep stages of sleep 3 and 4 delta sleep within 30 to 45 minutes after sleep onset. REM periods typically follow stages of deeper sleep, first appearing from about 70 to 90 minutes after sleep onset (Hauri, 1982).

As well as emitting characteristic low voltage electrical activity, the sleeping brain also has complex and distinct physiological processes. Hormones levels, such as growth hormones and prolactin, fluctuate depending on the stage of sleep. During sleep, reflexes change, cardiac output falls, digestive functions slow, respiration decreases, body temperature drops, and many other physiological systems are greatly influenced (Hauri, 1982).

Sleep is, therefore, regarded as an active and complex state with defined stages and cycles. We must understand sleep as it has pervasive influences on seizures. Sleep facilitates seizure activity, as well as serves a protective function (as shown by the production of seizures related to sleep deprivation). Changes in brain state (such as transitions from sleep to wakefulness) have significant consequences for seizure activity (Angelieri, 1975; Billiard, 1982; Montplaisir, Laverdiere, Saint-Hilaire, 1985; Passouant, 1982). Likewise, each sleep stage, REM and the four levels of NREM, can influence seizure activity (Passouant, 1982). The relationship between sleep and epilepsy is also reciprocal. Sleep disturbance results

from seizure activity, and seizure activity influences brain states (Baldy-Moulinier, 1982; Bittner-Manicka, 1976).

Sleep vs. Awake States

Sleep, relative to awake states, facilitates seizure activity. Sleep has a marked influence on the occurrence of generalized and partial seizures as well as on the frequency, morphology, and distribution of interictal discharges (seizure-like EEG patterns) (Montplaisir et al., 1982). Few individuals with epilepsy have seizures exclusively during sleep, and clinical epilepsy is much more commonly recognized for daytime seizures (Gibberd & Bateson, 1974). However, according to Hopkins (1933) and Janz (1962) 80% of epileptics experience seizures predominantly during sleep or on arousal from sleep.

Gibbs and Gibbs (1947) were the first to note that sleep will bring out abnormalities in patients' EEG, such as ictal discharges, seizures, and especially interictal discharges, that were not apparent when awake. Kellaway (1985) supports this observation by noting that spike activity that is not apparent during the day becomes distinct with the onset of sleep.

Neurologists have used the seizure promoting qualities of sleep to aid in the diagnosis of epilepsy. Sleep EEGs have been used by neurologists for decades to establish the status of patients suspected of having epilepsy. In an epileptic brain there is a high likelihood that seizure activity will be apparent during the first periods of sleep. Bridges & Ebersole (1987) recommend that only the first hour of a sleep EEG need be reviewed to establish epileptic status. Sleep EEGs have also been used to give a more reliable location of epileptogenic focus (Perria, Rosadini, Rossi, & Gentilomo, 1966).

A lack of sleep has also been shown to activate epileptic activity. Thirty to seventy percent of epileptic patients with normal routine waking EEG show ictal activity in waking and sleep EEGs after sleep deprivation (Baldy-Moulinier, 1982). (The influence of sleep deprivation and sleep loss on seizure activity is more extensively reviewed later in this proposal.)

While sleep can increase the likelihood of seizure activity, this is not true for all stages or cycles of sleep, nor is it true for all types of epilepsy. Most of the variance in seizure activity occurs between stages NREM and REM, and upon the transitions between waking and sleeping. There are also marked differences in the night-time seizure frequency depending on epilepsy type. Sleep and epilepsy are not unidimensional and much will be gained by a discussion of how specific sleep stages and cycles relate to seizure activity, and how specific types of epilepsy relate to night time seizure activity.

Sleep Stages & Seizures

Specific sleep stages are associated with seizure activity. Most seizures occur in NREM sleep; particularly stage 2 sleep (Baldy-Moulinier, 1982). Seizures are more likely to occur when an individual with epilepsy descends towards slow wave sleep and during the intermediary stages following REM (Halsz, 1982; Kellaway, 1985).

Several researchers suggest that the deeper the stage of NREM (such as, stage 3 or 4) the less the likelihood of seizure activity. Halsz (1981) found the deeper the stage of sleep, the greater the resistance to seizures evoked by sensory stimulation. Daytime epileptics, who seldom or never experience night time seizures, have an increased proportion of delta sleep compared to normals (Biniaurishvili & Yakhno, 1982).

REM is a stage of sleep that appears to inhibit seizure production (Shouse, 1986). Paroxysmal activity (i.e. spike-form EEG) almost always decreases during REM (Bittner-Manicka, 1976; Kellaway, 1985). However, exceptions have been noted where REM sleep appears to promote seizure activity (for example, Bittner-Manicka, 1976). Passouant (1967) states that REM sleep increases focal seizures, particularly temporal lobe discharges.

Sleep-Wake Cycle and Seizures

Relationships between the sleep-wake cycle and seizures have been observed. The sleep-wake seizure pattern for individuals with epilepsy is typically consistent. Seldom do those who experience their seizures mostly at night develop daytime seizures. Those who

experience seizures throughout the day and night seldom deviate from this pattern (Gibberd & Bateson, 1974).

Sleep epilepsy

Sleep epilepsy (also called nocturnal or night-time epilepsy) is classified by a predominance of seizures occurring at night, during sleep. Few individuals with epilepsy have seizures exclusively during sleep (Gibberd & Bateson, 1974). However, some estimates claim as many as 80% of epileptics have seizures mostly during sleep or while waking from sleep (Hopkins, 1933; Janz, 1962).

About half of all sleep epilepsy results in generalized or complex partial seizures (Baldy-Moulinier, 1982). The high proportion of generalized seizures may be an artifact of the detectability of such seizures. If the type of epilepsy does not have tonic-clonic convulsions, then it may be overlooked as occurring at night. The detection of seizures without tonic-clonic convulsions usually requires an all night sleep polygraph (Shouse, 1986).

Night time epilepsy can develop at any age (Shouse, 1986). Most sleep epilepsies are relatively benign and most individuals remain free of obvious neurological damage, and deficits in cognitive functioning, even after many years of nightly generalized seizures (Gibberd & Bateson, 1974). There are many reports of normal daytime EEGs in patients with nocturnal seizures (for example, Bittner-Manicka, 1976). Others have found more disturbed daytime EEGs in those with nocturnal seizures (Gibberd & Bateson, 1974). As a group, patients with pure sleep epilepsy have a good prognosis (Montplaisir et al., 1982).

With night epilepsy, seizures come when first sinking into deep sleep and in the early morning (Gilbert & Bateson, 1974; Montplaisir et al., 1985). The most frequent seizure times for nocturnal epilepsy are from 10-11 p.m. (12 p.m. in some patients older than 15, or who have a long history of seizures), and from 4-5 am. The precise peaks may vary depending on the patient's bedtime and waking schedule (Montplaisir et al., 1985; Shouse,

1986). Most sleep epilepsy attacks usually appear without any exogenous triggering (Vieth, 1986).

The EEGs of nocturnal epilepsy have been investigated by many research groups, with contrasting findings. Biniaurishvili & Yakhno (1982) note that individuals with nocturnal epilepsy have greater stage 2 sleep than normals or individuals with mostly daytime seizures. Baldy-Monlinier et al. (in Vieth, 1986) state that stages 1 and 2 predominate, and there are shorter periods of 3 and 4, and more wake-ups. When seizures occur early in the sleep period, REM sleep may be suppressed (Besset, 1982). Other groups have found night seizures to have increased proportion of stages 3 and 4 compared to normals. Vieth (1986) describes the sleep of night epileptics as too profound, having few sleep spindles and excessive deep NREM during which seizures are prominent.

Awakening epilepsy

Awakening or arousal transitions in sleep stages can activate seizures. In 90% of awakening epilepsy the seizures are generalized (Baldy-Moulinier, 1982). Awakening seizures are often considered hereditary or idiopathic and frequently appear to have an age dependent course (Baldy-Moulinier, 1982; Shouse, 1986).

Daytime epilepsy

Individuals with only daytime seizures have been reported to have an increase of delta-sleep (Biniaurishvili & Yakhno, 1982). Bekhtereva and colleagues (1978) believe that an increase in delta-sleep may serve a kind of protective function against seizures occurring during sleep.

Diffuse epilepsy

Diffuse epilepsy is not entrained to the sleep-wake cycle but describes seizures occurring randomly throughout the day and night. Diffuse epilepsy is evenly distributed across the age spectrum (Shouse, 1986). Very serious sleep abnormalities are seen in persons with diffuse epilepsy, especially those with significant neurological impairment; in most cases there is a known organic basis for the epilepsy. The prognosis for individuals

with diffuse seizures is poor; they tend to respond poorly to anticonvulsant medication (Shouse, 1986).

Seizure Types & Sleep

Generalized seizures and sleep

The most profound effects of sleep on seizure activity are manifest in patients with generalized epilepsy (Gabor & Seyal, 1986). Generalized seizures usually awaken the patient. It is not clear if the arousal from sleep triggers the seizure or the seizure causes an arousal from sleep (Montplaisir et al., 1985). Repeated generalized seizures can cause the EEG to become so uniform throughout the night that criteria cannot be used to score sleep stages. The ultradian rhythm of REM may be also be abolished (Besset, 1982; Passouant et al., 1976).

Patients with generalized seizures have seizures that are closely related to sleep (Montplaisir et al., 1982), and 30% of individuals with generalized seizures have pure sleep epilepsy (Billiard, 1982). Generalized seizures are likely at the end of slow wave sleep (Gibberd & Bateson, 1974), or occur in relaxed waking (Biniaurishvili & Yakhno, 1982). The peak times for seizure occurrence are 1-2 hours after sleep onset and 5-6 a.m., and almost always occur in NREM (Besset, 1982; Passouant et al., 1976).

Frequent nocturnal generalized seizures can lead to chronic REM sleep deprivation, which in turn may cause increased neuronal excitability, and reduce the seizure threshold (Bowersox & Drucker-Colin, 1982). Surprisingly, generalized seizures can happen on a nightly basis for several years without obvious neurological damage or impairment to cognitive functioning (Montplaisir et al., 1982).

Partial seizures and sleep

Partial seizures occur mostly during the day (Billiard, 1982; D'Allesandro, Sintini, Pazzaglia, & Lugaresi, 1983), although the number of nocturnal seizures may be underestimated since partial seizures in sleep often go undetected, even by trained nurses (Passouant et al., 1975).

Partial seizures appear to have a unique relationship to REM stage sleep. With most types of epilepsy, REM acts to reduce seizure activity; however, in partial epilepsy REM appears to increase seizure activity. Gibberd & Bateson (1974) report that focal seizures tend to happen during REM. It may be, however, that REM makes partial seizures more apparent by inhibiting a more generalized spread. Studies show maximal focalization for partial epilepsy during REM (Perria et al., 1966; Ross, Johnson, & Walter, 1966; Hess, 1974; Lieb, Joseph, Engel, & Crandal, 1980; Montplaisir, Saint-Hilaire, Laverdiere, Walsh, & Bouvier, 1980).

There is debate over the activating characteristics of REM for partial epilepsy. Cadilhac (1982) showed that temporal lobe seizures are activated in REM sleep. Several studies have also shown that ictal discharges increase during REM (Passouant, Cadilhac, & Delange, 1965; Epstein & Hill, 1966; Mayersdorf & Wilder, 1974). Similar results have been produced in animal studies (for example, Arias & Passouant; 1971, Frank & Pelgrani, 1974). However, these findings come from surface electrode studies and several depth electrode studies (animal and human) have found a reduction in firing during REM for temporal lobe epilepsy (Laverdiere, Montplaisir, & Saint-Hilaire, 1984; Mayanagi, 1977; Lieb et al., 1980)

Absence seizures and sleep

Absence seizures are common in childhood and are characterized by a brief absence or lapse of consciousness, lasting about 5 to 20 seconds (Niedermeyer, 1990). Absence seizures occur almost exclusively on the borderline between sleep and wakefulness. A few cases of absence seizure forms have been noted in REM sleep (Gaustaut & Broughton, 1965; Patry, Lyagoubi, & Tassinari, 1971). Absence seizures are seen almost entirely during wakefulness. There are seldom behavioral correlates of absence seizure discharges in sleep (Ross et al., 1966 ; Montplaisir et al., 1985). Niedermeyer (1965) reports observing a fluttering of the eyelids of absence epileptics during sleep. Polygraph evidence exists of 3

Hz spike and slow wave seizure discharges in absence seizure patients when the patient becomes drowsy or falls asleep (Montplaisir et al., 1982).

Interictal discharges and sleep

Interictal discharges (IIDs) are EEG discharges that occur between seizures; they can be more prevalent during sleep than ictal (seizure) events (Shouse, 1986). Interictal discharges, like seizures, are common in NREM (Shouse, 1986). Normally IID's increase in NREM sleep and decrease or disappear in REM sleep (Gastaut & Broughton, 1965; Ross et al., 1966; Passouant, 1967; Billiard, 1982). In most patients IIDs are more prominent at sleep onset and during the first part of night (Montplaisir et al., 1982). Some patients are selective for epileptiform activity during the last part of the sleep cycle. Seizures may be more likely at this time because the blood-serum level of anticonvulsant medications may be at their lowest level (Montplaisir et al., 1982).

Seizures Influencing Sleep

Several sleep disturbances have been reported by people with epilepsy and there is some evidence that sleep disturbance and epilepsy may aggravate and perpetuate one another (Besset, 1982; Declerck, Wanquir, Sijben-Kiggen, & Martens, 1982; Delange, Castan, Cadilhac, & Passouant, 1962; Hamel & Sterman, 1982; Kikuchi, 1969; Montplaisir et al., 1980; Montplaisir et al., 1982). Epilepsy frequently alters sleep patterns. Nocturnal generalized seizures disrupt sleep so profoundly that, in severe cases, the different stages of NREM sleep can no longer be identified (Baldy-Moulinier, 1982). Partial seizures and interictal epileptiform patterns may also disturb sleep (Montplaisir et al., 1982; Hoeppner, Garron, & Cartwrite, 1984). Very serious sleep abnormalities are seen in persons with diffuse epilepsy, especially those with significant neurological impairment (Shouse, 1986). Hoeppner, et al. (1984) found a significant positive correlation between seizure frequency and sleep problems. Similarly, Sterman, Shouse, & Passouant (1982) found the severity of the disorder is positively correlated with the severity of the sleep deficits.

Disturbances of sleep appear to interrelate with epilepsy (Besset, 1982; Declerck et al., 1982; Delange, Caston, Cadilhac, & Passouant, 1962; Hamel & Sterman, 1982; Kikuchi, 1969; Montplaisir et al., 1980; Montplaisir et al., 1982; Shouse, 1986; Passouant et al., 1965), and these disturbances occur whether the seizures occur in waking or sleep states (Baldy-Moulinier, 1982; Shouse, 1986).

These sleep disturbances include:

1. increased sleep latency
2. increased light sleep (stage 1 & 2 NREM sleep)
3. decreased K complexes
4. increased number and duration of awakening after sleep onset
5. increased shifting between sleep stages
6. decreased stages 3 & 4 NREM
7. decreased and fragmented REM
8. decreased sleep efficiency

Abnormal or disturbed sleep may help the expression of epileptic activity. It is also possible that sleep disturbance and epilepsy share a common neuroanatomical substrate. Hamel & Sterman (1982) found in kindled[1] cats that sleep disturbances precede EEG and behavioral seizures. Sleep deprivation may augment seizure activity by compounding existing sleep abnormalities (Shouse, 1986).

Sleep and Seizure Mechanisms

The previous discussion has described neuropsychological research and clinical findings of the interrelationship of sleep and epilepsy. The descriptive approach of these disciplines does not provide a biologically oriented explanation of the possible mechanisms involved; specifically, what neurophysiological and neurochemical processes occur by which sleep actually influences, and is influenced by, brain seizure activity.

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[1] Kindling is a surgical procedure whereby the cortex is lesioned or treated, such as with aluminium paste, making seizure occurance more likely.

The basic mechanisms of epileptic activity are extremely complex and our insights have remained fragmentary (Niedermeyer, 1990). The accepted model of seizure genesis is that seizures arise as a result of brain damage or a change in the physiology of the brain. The following is a review of such a model. (It should be noted that there are opponents to such models. For example, Fenwick (1990) and Dahl (1993) criticize the model as being too simplistic, omitting the influence of many environmental, behavioral, and psychological factors.)

Seizures and sleep structures

Jackson (1931) proposed that seizures came from specific lesions in the cortex. However, this has never explained seizures that had no specific focus, no indication of a specific local brain malfunction, or that appeared genetically determined. The thalamus, as a midline structure, was later thought to be responsible for non-specific seizures, and several experiments indicated thalamic involvement in seizures (Angyan, Katjtar, & Sik, 1967; Guerrero-Figureoa, Barros, De Balbian-Vester, 1963; Ingvar, 1955; Jasper & Droogleever-Fortuyn, 1947; Lewy & Gammon, 1940; Pollen, Pero, & Reid, 1963).

Schools of thought also supported a cortical origin for seizures, as several studies showed hemispheric differences that indicated other than a centrally located thalamic based seizure mechanism (Gibbs & Gibbs, 1952; Testa & Gloor, 1975). In time, the debate between adherents of either cortical or thalamic origins became meaningless as seizures could obviously be triggered from either the thalamus or the cortical pole of the non-specific thalamo-cortical system (Halasz, 1982).

Several studies have shown that sleep regulating structures exist in the cortex, and in the thalamus, and that these regions are also related to seizure activity. Hess (1954) identified a sleep center in the thalamus. Previously, Jasper and Hess (1953) had stimulated this area which generated spike-wave patterns. Villablanca, Schlag, & Marcus (1970) also showed that a region of the forebrain, when lesioned could cause insomnia, disturbed slow wave sleep, and reduced cortical spike-waves. Further studies indicate that structures

responsible for sleep and for the generation of spike-wave epilepsy, are related (Feeney & Gullotta, 1972; Junko, Andy, & Webster, 1971; Madoz & Reinoso-Suarez, 1968).

Sleep promotion and arousal

A reciprocal induction regulation model, developed by Selbach (1962) and adapted by Halasz (1982) describes the sleep-wake process and provides a valuable framework to examine seizure mechanisms. Previous models (Moruzzi, 1972; Bremer, 1975) describe falling asleep as an antagonistic process, where the sleep promotion system combats the reticular activation system (RAS) to allow sleep to occur. In other words, sleep occurs despite the RAS (Halasz, 1982). In contrast, the reciprocal induction regulation model (Halansz; Selbach) suggests that two mutually antagonistic "half-systems" cooperate in such a way that a stimulus in one system causes a reciprocal induction (not inhibition), of the opposite system. Thus, stimulation of one system produces a rebound in the other, again activating the first system, and so on.

This is an attractive model for it is consistent with the micro-oscillations present in sleep: there are constant fluctuations of the depth of sleep in all its phases. A sudden change in any direction of sleep is followed by a correction in the opposite direction. K-complexes have been considered to be abortive arousal responses or to represent a protective sleep function. Whatever their function, they appear (at least to Halasz) as tracer marks of the phasic interaction—the clashes between the two systems.

Niedermeyer (1972) suggests that fluctuations in sleep stages may aid in the development of seizures. Observing that spike-wave paroxysms occur frequently in association with arousal stimuli (and K-complexes, which are interpreted as abortive arousal responses), he proposed that generalized seizure activity is the consequence of an error in the arousal mechanism. Seizures are therefore a kind of overshoot of a normal arousal mechanism. This is consistent with the understanding of sleep as a constant interplay of arousal and hypnotic mechanisms. It is also consistent with the similarities between the timing of K-complexes and sleep spindles and the occurrence of spike-waves and seizures.

Where Niedermeyer considered spike and seizure activity to be the result of a disordered arousal mechanism, Halasz (1982) adopting the reciprocal induction regulation model, considered that it is an epileptic malfunction of the sleep promoting mechanism. According to Halansz, generalized seizures occur because the resultant arousal reaction to the sleep promotion force was overshot.

The significance for this distinction becomes clear as the focus for understanding seizure inducing circumstances shifts from factors that cause excessive arousal to those that create excessive pressure on the sleep promotion system. Environmental influences that reduce the tone of the reticular arousal system are essential factors in provoking seizure phenomena as reduced arousal opens the way for epileptic malfunction of the sleep promoting system. On the other hand, those factors which improve the tone of the arousal system have an inhibiting effect on seizures (Neill & Alvarez, 1989). States of extreme wakefulness and deeper sleep, in comparison, are not conducive to seizures. This is supported by clinical findings that indicate that an increase in vigilance is associated with a decrease in seizure occurrence (Dahl, 1993).

Vigilance changes

Laboratory and clinical findings converge to suggest that a state of reduced vigilance is central to the relationship of sleep and seizure activity in epileptics. There are optimal zones of superficially reduced vigilance, towards waking, and towards deep sleep, which favor the appearance of seizures. Such zones can result from falling asleep, momentary awakenings during the night, transitions between REM and slow wave sleep, and drowsiness while waking in the morning (Lennox, Gibbs, & Gibbs, 1936; Halansz, 1982). Reduced vigilance can also be the result of environmental events, physiological events (including the influence of benzodiazapines), and a seizure itself (Halansz, 1982).

Many of the influences that trigger seizures may do so by promoting a reduction in the level of vigilance; that, in turn, produces or perpetuates a brain state conducive to seizures (Halanz, 1982; Vieth, 1986). That sensory stimuli can induce epileptic seizures may be

partially explained by Vieth (1986) who suggests that during lower levels of vigilance, neuronal activity is more synchronized than at higher levels, and thus stimuli may have more success in evoking an epileptic seizure. Stimulation may trigger seizures when single or rhythmic stimulation of afferents get the already stimulated neuronal system oscillating.

Increasing vigilance appears to have an inhibiting effect on seizures. Studies have found that arousing stimuli and focusing attention inhibits spike wave patterns and absence seizures (Jung, 1954; Neill & Alvarez, 1989). Sterman and colleagues (1984) have repeatedly demonstrated that seizure thresholds are elevated when an individual with epilepsy is instrumentally trained to produce spectral EEG bands that reflect a vigilant waking state (12 to 15 Hz). Animal studies have found that direct stimulation of the RAS also inhibits spike wave pattern and absence seizures (Guerrero-Figureoa et al., 1963; Pollen et al., 1963).

These findings are consistent with the clinical observation that the most general seizure avoiding mechanism by a patient is increasing alertness. A well known case study, that may have involved such a strategy, was that of Efron (1956) who encouraged a woman with epilepsy to focus her attention on a silver bracelet. This attention is believed to have caused the patient's subsequent decline in seizure frequency.

Sleep, Flight, and Seizure Risk

The interrelationship of sleep and epilepsy, reviewed above, suggest that stages of sleep and types of epilepsy can combine to put an individual with epilepsy at increased risk for seizures. Most individuals with epilepsy appear to have a greater likelihood of experiencing seizures around fluctuations of consciousness associated with sleep: the brief period of falling asleep in the evening (for example Wyler, 1974), light sleep around momentary awakenings during night (for example Niedermeyer, 1972), intermediary sleep between REM and slow wave sleep (e.g., Kellaway, 1985), or awakening in the morning while still drowsy (Biniaurishvili & Yakhno, 1982). Seizures are most likely at night when first falling into deep sleep and in the early morning (e.g., Besset, 1982). Sleep and vigilance

related seizures may be more common in those with generalized epilepsy (Gabor & Seyal, 1986). It has been shown that those individuals with epilepsy and sleep disorders, such as disorders of initiating or maintaining sleep, or those who experience transient sleep loss, will also be at increased risk for seizure occurrence (e.g., Montplaisir et al., 1982).

As periods where there is a level of slightly reduced vigilance are likely to place an epileptic at increased risk for seizures, it would be detrimental for individuals with epilepsy to be exposed to prolonged periods of monotonous, boring, and wearisome activity. Such activities have favored the occurrence of daytime seizures (Neill & Alvarez, 1989). In telemetry observations daytime seizures are concentrated around stages marked by a slight transitional drop in the level of vigilance (Bureau, Guey, & Dravet, 1968).

Air travel may often be monotonous, boring, and wearisome. Airplane passengers spend most of their travel time seated, in a fixed environment with a limited range of stimuli and activities. Air travel, layovers, and airport transitions may last for days. Such soporific circumstances are likely to produce drowsiness and a reduction in vigilance. In addition, flights that involve transmeridian desynchronosis are likely to result in sleep loss and sleep disruption. As previously noted, these consequences to flight are also likely to contribute to a lowering of seizure threshold.

Sleep Loss and Epilepsy

As previously noted, air travel has been associated with sleep loss (Nicholson, 1972). The following is a review of how sleep loss, as a consequence of air travel, may promote seizures. Neurologists have long suspected that loss of sleep or irregularity of the sleep-wake cycle might contribute to the production or precipitation of seizures in some individuals (Gunderson, Dunne, & Feyer, 1973; Lennox, 1955; Merritt, 1967). There is little experimental evidence to support that sleep loss is related to seizures in non-epileptics (Bennett, Ziter, & Liske, 1969; Cohen & Dement, 1965; Mattson, Pratt, & Calverley, 1965; Rodin, Luby, & Gottlieb, 1962). The relationship of sleep loss and seizures in non-epileptic populations has never been established (Gunderson et al., 1973). However, for epileptic populations the relationship between sleep loss and decreased seizure threshold has been repeatedly confirmed.

Defining Sleep Loss

Some individuals appear to require very little sleep. Jones and Oswald (1968) report two cases where individuals slept only about 3 hours each night without sleep complaints. Meddis, Pearson, & Langford (1973) report of a 70 year old woman who slept on the average of one hour each night with no daytime naps and was reported alert, competent, with no need or desire for more sleep.

The question arises, with such individual variability, what is adequate sleep and how is sleep loss defined? There are no established standards to assess how much deviation from mean sleep times constitutes a loss, nor are there standards for defining a routine sleep regimen. It is also more difficult to establish sleep loss for an individual with a varied sleep pattern. Specifically, it is not known whether a particularly brief sleep is the result of normal variability, or whether it represents a sleep loss. Another unaddressed issue is whether sleep loss is specific to a previously established circadian pattern. For instance, does a shift in sleeping times (but not amount of sleep) constitute a loss? Literature on sleep deprivation and sleep loss seldom address these issues. Sleep loss is typically defined as

any decrease in sleep time for a given period, usually 24 hours. In a review of sleep deprivation studies, Johnson (1969) states that with wide variability of the amounts that individuals typically sleep, the important reference point is the restriction of the usual sleep regimen and not the amount of sleep; sleep loss is thus self-referenced.

Experimentally, sleep has been totally restricted, partially restricted, and restricted by specific stages to assess the effects of sleep loss. Studies have also been done on individuals whose occupation regularly exposes them to sleep disruption and sleep loss.

Partial Sleep Deprivation

Non-epileptic subjects and sleep deprivation

There are specific neurological changes with partial sleep loss with non-epileptic subjects. While there is no change in their awake EEG, there are several changes in their sleep EEG (Johnson, 1969). If the subject's sleep was less than five hours then there is frequently an increase of slow wave sleep and a decrease in REM. (REM will have an earlier onset with prolonged loss.) There will also be a reduction of stages 1 & 2 (Johnson, 1969; Webb & Agnew, 1965; Sampson, 1965).

Partial sleep loss shows only mild impairment, and occasional improvements in behavior. Some decrements in task performances were documented after partial sleep deprivation of 1.5 hours for the first night, 3.5 hours for the second night, and 5.5 hours for the third night (Lubin & Williams, 1959). Vigilance impairment to an auditory stimulus was apparent with partial sleep deprivation of two hours for the first night, and five hours for a second and third night (Naitoh & Dement, 1975). Webb & Agnew (1965) conclude that sleepers, accustomed to 7 or 8 hours of sleep per night, can maintain 5 to 6 hours of sleep per night for as long as two months, with little or no decrement in performance. Sleep can be shortened without serious disruption of waking activities, and humans perform quite well without entering into all stages of sleep or with only limited amounts of each stage. A subject's response to sleep loss depends on their age, physical condition, mental health,

expectations of others, whether drugs or stimulants are used to maintain wakefulness, and the support of others (Johnson, 1969).

Considerable evidence has been amassed to refute the notion that sleep loss will cause seizures in non-epileptics. Total sleep deprivation, sometimes as much as 264 hours, did not induce epileptiform discharges in healthy subjects (Jovanavic, 1967; Heinemann, 1966; Johnson, 1969; Naitoh, Kales, Kollar, Smith, & Jacobson, 1969).

Epileptic subjects and sleep deprivation

Often patients only show epileptic potentials in their EEG after sleep deprivation. In patients with epilepsy (of awakening) there is an enormous augmentation of paroxysmal discharges after a sleep deficit, which further increases as the period of poor sleep progresses. In these patients the period of greatest risk of a clinical seizure exists between 5 and 7 a.m. (Jovanovic, 1967). Bechinger and Kornhuber (1976) found that sleep deprivation was better at promoting absence and partial seizures, rather than generalized seizures.

Although the pathophysiological mechanism responsible for seizures has not been established, it is known that the recruitability of neurons, and the number of neuronal elements which can be activated by exogenous stimulation, is highest during fluctuations of vigilance (Speckman & Caspers, 1973; Scollo-Lavizzari, Pralle, & Radue, 1977). Jouvet (1969) focuses on neurochemical mechanisms, explaining that sleep deprivation induces a change in the relation of biogenic amines which promote seizures. Pompeiano (1969) posits that sleep deprivation causes neurophysiological changes that in turn promote seizures. Bergonza, Chiurulla, & Cianchetti (1972) found that activation of hypersynchronous potentials occurred only after sleep deprivation of REM, but not after sleep deprivation of orthodox NREM.

Considerable attention has been given to the question of whether sleep deprivation has an activating effect that is due to the deprivation itself, or to the drowsiness that usually occurs (Berti-Ceroni, Sabattini, Gambi, & Lugaresi, 1967; Scollo-Lavizzari, et al., 1975).

Pratt, Mattson, Weikers, & Williams (1968) studied 118 epileptics (mostly adult males), and found that 41% had unequivocal activation due to sleep deprivation that was not the result of sampling effects. An additional sleep deprived EEG did not yield positive results simply because it provided an additional sample of the EEG.

There are no established incidence rates of clinical seizures to be predicted from sleep deprivation. However, Gunderson and colleagues (1973) and Degen (1980) demonstrated that it is possible to estimate the number of individuals susceptible to seizures after sleep deprivation in a population of apparently healthy young men (see below). Sleep deprivation studies typically lack controls that would make it possible to know how many seizures a population would have had without sleep deprivation. In a study by Degen (1980) among 788 subjects that underwent 12 to 28 hours of sleep deprivation, 19 clinical seizures occurred. Similar findings have been found by other investigators (Bechinger , Kriebel and Schlager, 1973; Rumpl, Lorenzi, Bauer, & Henge, 1977; and Tartara, Moglia, Manni, & Corbellini, 1980).

Flight related sleep deprivation and seizures

In non-epileptic populations, seizures seldom if ever result from prolonged sleep deprivation. Gunderson et al. (1973) observed that in returning servicemen, from Vietnam and other Southeast Asian posts, the prevalence rate for seizures (without neurological evidence of epilepsy) was one seizure per 10,000 subjects for 24 to 36 hours of sleep deprivation, and one seizure for every 2500 subjects if the sleep deprivation was two days or more.

Sleep deprivation that results from civilian air travel is seldom this long. For example, a transatlantic flight from New York to Frankfurt, Germany, most frequently departs in the early evening and arrives in the early morning (local time). By the time a traveler has left the terminal in Germany, it is about 3 a.m. New York time, and the traveler, even if he or she was unable to sleep on the plane, does not experience sleep

deprivation over 24 hours. Using Gunderson's incidence rates, a single seizure would be expected for every 10,000 non-epileptic passengers making this flight.

There are no reported seizure incidence rates for epileptics who experience flight related sleep deprivation. It is possible that air travel deprives an epileptic of sleep, similar to laboratory findings, and that this deprivation leads to an increase in seizures. This relationship is investigated in the current study.

Circadian Rhythm, Ultradian Rhythm and Epilepsy

Extended east-west air travel is likely to interrupt regular sleep patterns and sleep architecture, as well as numerous other biological rhythms. Sleep disruption and sleep loss may lead to an increase in seizures. Therefore, the study of circadian rhythm disruption may be key in understanding how air travel effects seizure threshold. The following is a review of biological rhythms, the processes of biological rhythm disruption and entrainment and their possible impact on seizure control.

Biological Rhythms

All animals have innate biological clocks that are reflected in sleep-wake cycles and daily feeding habits. Internal biological rhythms program our bodies to behave differently at different times of the day (Graeber, 1988). Well known examples of periodicities in our daily life are the day-night cycle, the wake-sleep cycle, the work-rest-cycle, and the menstrual cycle (Siegel, Siegfried, Gerathewohl, & Mohler, 1969). Biological timing of a circadian nature (approximately 24 hour cycle), can be shown in the daily oscillations of many physiological, biochemical, and behavioral variables (Samel & Wegmann, 1989).

Biological rhythms are seen as measurable physiological events such as body temperature, blood pressure, heart rate, sensory acuity, adrenal gland output, CNS neurotransmitter levels, excretion levels, and cell division (Luce, 1971; Moore-Ede, Sulzman, & Fuller, 1982). Psychological functions have also been determined to vary according to diurnal cycles, such as reaction time, decision time, critical-flicker, subjective fatigue, well being, and intellectual facility.

Exogenous rhythms

Exogenous rhythms exist as long as the environmental factors change periodically. Under normal conditions, biological rhythms exhibit periods corresponding exactly with the length of the day, suggesting that environmental cues trigger the timing of these rhythms.

While the body clock is inherently capable of monitoring the passage of time, it differs from most clocks in that its period is flexible (within a very limited range), and must therefore be properly set, or synchronized, before it can accurately predict the timing of periodic environmental events. This synchronization is accomplished through entrainment by external synchronizers or zeitgebers (time givers). When these environmental factors are no longer present, the periodicity fades (Graeber, 1988).

Zeitgebers can be environmental light/darkness, temperature, tidal, or geophysical forces. Changes in the hours of daylight and the temperature are the most effective zeitgebers (Aschoff, Hoffman, Pohl, & Wever, 1975). For humans, social time cues such as interpersonal communication, work schedules, or group activities are more important than cycles such as sunrise-sunset, ambient temperature, and food availability (Moore-Ede et al., 1982; Wever, 1979).

Endogenous rhythms

Most body rhythms run autonomously when all environmental time cues are excluded. Thus, most human circadian rhythms are of an endogenous nature. Periodicity depends on the organism, the environment merely influences the onset of the phase. If the exogenous and endogenous periods are similar, the entrainment process adjusts the inner clock to the environmental cycle by showing a definite phase relation between the oscillations of the organism and the exogenous periodicity (Hoffman, 1965).

Studies of endogenous rhythms have been done in time isolation laboratories where all external zeitgebers are either removed or carefully manipulated. Such control allows for the body clock to reveal its natural operating characteristics uncontaminated by time cues,

that is, to run freely. Under such conditions the human circadian system consistently behaves as if it is controlled by not one but two biological clocks (Graeber, 1988). Kellaway, Frost, & Crawley (1980) describe two rhythmic processes, an ultradian cycle of 100 minutes, (such as the sleep stage cycle), and a second circadian cycle of approximately 24 hours (such as the biological rhythms attuned to the day-night cycle).

Volunteer subjects living in temporal isolation for several weeks begin sleeping and waking on a 24 hour schedule but soon spontaneously lengthen their day up to as long as 48 hours without any awareness of doing so (Colin, Timbal, Boutelier, Houda, & Siffre, 1968; Wever, 1979). The body temperature cycle is much more resistant to extension, it extends to about 25 hours and remains there despite the much longer rest-activity cycle.

Timing of sleep and body temperature

The duration and quality of sleep depends on when sleep occurs within the body temperature cycle (Graeber, 1988). Subjects sleep for longer periods when they go to sleep near their temperature peak (their temperature is falling or soon falling) and for shorter periods when they retire near the temperature trough (their temperature is rising or soon rising). It is the timing of sleep, and not the amount of time awake, that is critical factor controlling sleep duration (Hauri, 1982).

REM sleep is typically coupled to the temperature trough. Going to sleep near the peak results in most REM sleep occurring in the second half of sleep. Conversely, going to sleep while your body temperature is low increases the likelihood of having REM in the first half of sleep (Czeisler, Weitzman, Moore-Ede, Zimmerman, & Knauer, 1980; Zulley, Wever, & Aschoff, 1981). The quality of sleep is therefore affected by when sleep is attempted relative to the circadian rhythm of body temperature. Sleeping for long times may be more a function of timing of sleep (that is, when body temperature rhythm is falling) than the consequence of fatigue or time awake. The most difficult time to try sleeping is when body temperature is rising. An individual will have considerably more difficulty getting to sleep, and if successful will usually waken within a relatively short time.

Individuals with epilepsy may be prone to seizures when experiencing prolonged periods of drowsiness. Therefore, it may be beneficial for individuals with epilepsy who are flying to only attempt sleep when their temperature is falling. In this regard it may be helpful to monitor temperature rhythms and plan sleep times. Optimal sleep during layovers depends on when the sleep is attempted; the timing, and the adequacy of accommodations, for getting sleep, may be more important than the layover length. (As an apparent oversight, policies that establish layover time required by flight crews do not adjust for temperature cycles.)

Sleepiness as a circadian rhythm

There is a consistent rhythm in our tendency to fall asleep, even during daytime hours when individuals are living according to their normal routines. Falling asleep occurs more quickly in the afternoon, and at night, regardless of age, and regardless of underlying levels of sleepiness (Richardson, Carskadon, Orav, & Dement, 1982). These findings are based on the Multiple Sleep Latency Test (MSLT) where there is a removal of all external stimuli (soporific environment) and the patient is instructed to remain in bed and to try to sleep. The MSLT is stopped after the first 90 seconds of EEG-validated sleep, or after 20 minutes. Ultradian rhythms may also influence seizure frequency. Stevens, Kodama, Lonsbury, & Mills (1971) documented cyclic suppression of cortical activity on a 90 minute basis that corresponds to REM periods, and that also extends into wakefulness.

Diminished periods of vigilance are "danger periods" for individuals with epilepsy. During periods of sleepiness, cortical cell assemblies are more prone to become synchronous and fire epileptically. Therefore, periods in the afternoon and evening present a greater risk period for seizure occurrence.

Circadian Rhythm Disruption

The disruption of circadian rhythms has been associated with discomfort and ill health for centuries. The adverse effects of unusual schedules on the individual's subjective and physical state are noted in the Declaration of Independence. A grievance against King

George III is as follows: "He has called together legislative bodies at places unusual, uncomfortable, and distant...for the sole purpose of fatiguing them." (Seigel et al., 1969, p.1249).

Changing daily cycles makes physical and psychological demands that are often perceived as unpleasant. History supplies us with an interesting example of how resistant societies can be to change in their daily cycles. In the Journal of Paris in 1784, Benjamin Franklin published the suggestion to turn back our clocks in the summertime to arise earlier. It was not until the 20th. century that this suggestion was taken up and called "daylight savings time" (Seigel, et al., 1969).

Western civilization has introduced disruptions to the naturally occurring circadian rhythms. Before the widespread use of electric lights, humans typically lived in harmony with their circadian system, working during the day and sleeping at night; however this pattern is much less common today. Each year increasing numbers of shift workers must work at times that conflict with their circadian rhythms (Graeber, 1988). Air travel is an increasingly accessible mode of transportation that presents opportunities for time-zone related circadian rhythm disruption; physiological functions become locked upon another periodic system (Seigel et al., 1969). Space travel has also been shown to result in delays of physiologic cycle correspondence, with symptoms of fatigue, urinary irregularity, appetite changes, and major disruptions of sleep-waking patterns (Siegel, et al. 1969).

Circadian rhythm disruptions have been documented to have serious health and safety consequences. In the field of occupational medicine there is a large body of literature indicating health hazards in situations involving repeated reversals of sleep-wake patterns (Weitzmann, Kripke, Goldmacher, McGregor, & Nogeire, 1970). Effects from rapid sleep-wake cycle shift caused by industrial work shifts and geographical time-zone shifts include alterations in psychological function, work efficiency, and somatic symptoms (Hauty & Adams, 1966; Menzel, 1962; Solberger, 1966; Weitzman et al., 1970). The list of occupations where rapid shifts of circadian rhythm occur is long: airline pilots and crew,

maintenance and traffic control personnel, hospital medical and psychological staff, commercial drivers, police and fire department workers, hotel personnel, new parents, and many others. If challenges to circadian rhythms are related to increased seizure frequency, there would be additional concern for the health and safety of individuals with epilepsy involved with transmeridian travel or shift work.

Research programs at Baylor University and research in Aerospace Medicine have involved the artificial manipulation of the light/dark ration to determine the effects of changes on the body's circadian rhythms. Weitzmann et al. (1970) inverted the day-sleep cycle by keeping subjects up one night and changing sleep patterns to be 12 hours ahead, that is, subjects slept during the day. With this design it was assumed that subjects slept the same amount, but slept out of phase with their regular circadian rhythm. Results indicated that the basic 90-100 minute cycle was preserved but significant changes occurred in the duration, stability, and timing of the sleep stages. Weitzmann's subjects slept less, had increased stage 1 sleep, experienced REM earlier, had decreased REM and had increased waking from REM. Subjects also experienced an increase in the number of changes of sleep stages, and an increase in waking in the latter one-third of sleep. Weitzmann concludes: " Our findings of a significant delay in the re-establishment of normal sleep patterns indicate the possible importance of correlating sleep-stage changes to specific occupational work-rest cycle changes. Monitoring sleep patterns and other physiological variables with cycle shift experiments may lead to more rational schedules for work-activity patterns." (p.488).

Da Silva, Aarts, & Binnie (1984) suggest that interictal epileptic EEG activity corresponds to fluctuations of circadian rhythms, and that patterns of circadian and ultradian rhythms influence seizure frequency independent from sleep/wake or REM/NREM. The circadian rhythms observed to influence epileptic EEG activity are secondary to the direct action of the sleep-wake rhythm (DaSilva et al., 1984). There is no evidence of an endogenously driven circadian rhythm that influences seizures. One reason

for this lack of evidence may be that once antiepileptic drugs are in a therapeutic range there is no relationship between circadian fluctuations and increases in ictal frequency. It is difficult to isolate the impact of endogenous rhythms on seizure frequency from the influence of other factors such as activity and antiepileptic drugs.

Time Zones, Desynchronosis and Flight

Air travel is most disruptive to sleep and other biological and behavioral rhythms when it is transmeridian. The current section reviews circadian rhythm disruption specific to east-west flight.

Time-Zone History

Until the late 1800s, no standard time zones existed, individual towns would estimate noon as best they could by trying to determine when the sun was directly overhead. There were more than 100 different time zones in the United States! The state of Michigan had 27 time zones! (Corliss, 1949). Modern transportation gave rise to the need to create a standardized time system. The U.S. railroads, needing a uniform system as a basis for establishing train schedules, established an informal system of 4 time zones across the US. that was officially adopted by congress in 1918 (Siegel et al., 1969).

Circadian rhythm became a matter of importance to travelers with the evolution of the airplane and the feasibility of long distance flights, especially since the introduction of jet powered transportation introduced in the late 1950s (Siegel et al., 1969). Examples of early encounters with the effects of extended flight include Charles Lindburgh's 1927 New York to Paris flight, where he fell asleep and woke to find himself descending toward the Atlantic. Wiley Post readjusted his daily living pattern before his departure to match Moscow time, the midway point of his pioneering global flight (Post & Gatty, 1931).

In the early days of aviation, fatigue was viewed as a function of total flight time and workload intensity. Such a view was reasonable considering that most flying was accomplished during the day. The advent of frequent night flying and transoceanic aircraft made it necessary to consider the influence of biological rhythmicity on flight performance (Graeber, 1988).

A modern example of the effect of extended flight on flight crews biological rhythmicity is a study by Carruthers, Arguelles, and Mosovich (1976). Analysis of the EEG monitoring revealed that during the early morning hours (4 a.m. to 6 a.m.) while the

airplane was cruising on autopilot, all five on-duty crew members displayed various brainwave patterns characteristic of sleep, or extreme drowsiness, including sleep spindles, and increased 12-14 HZ activity with mass EEG synchronization!

Research designs have investigated actual flights as well as simulated flight conditions. Most research about the effects of multiple time zones flight on circadian rhythms has been carried out on non-pilot subjects flying as passengers. (For reviews see Graeber, 1982; Klein & Wegmann, 1980). Most studies have focused on readily available student subjects.

International attention has been paid to the impact of extended flight. Britain's Royal Air Force recognized that stress and transmeridian desynchronosis, can combine to dangerously impair performance (Howitt, Balkwill, Whiteside, & Whittingham, 1956: 1965). In 1967 the British Board of Trade mandated that any pilot of a British registered aircraft document that minimum rest periods have been established. If there was a time zone change of 4 or more hours between place of departure and place where the duty ends, the following rest period should not be less than 12 hours (Her Majesty's Stationary Office, 1967).

Germans monitoring their North Atlantic route found that the greater the interval between the time of departure and the maximum activity of the pilot, the greater the stress. Intercontinental flight crews have since been scheduled with consideration to departure time, flight duration, and multiple landings (Klein, 1968).

French researchers found that with their Paris to New York route (5 time zones), the younger pilots suffered less from fatigue than older pilots. The French established a policy where East-West-East flights be given more flight credit than North-South flights. In a Paris to Alaska route researchers found circadian variations of 17-OH Corticosteroids. A four hour shift in the rhythm of several biological functions occurred after a five-hour shift in time. A ten-hour shift was more physiologically disrupting than a five hour time shifts done twice (Ghata, Fourn, & Borrey, 1967).

Dutch researchers investigated the effects of a flight route from Amsterdam to New York, from New York to Alaska, and finally from Alaska to Tokyo. After arriving in New York the flight crew rested for four days, during this time most of their circadian rhythms did not become entrained to the New York day-night cycle. The amplitude of the rhythms for excretion of water and electrolytes decreased. Flying as far as Alaska shifted the excretion maximum and there were depressed amplitudes of water and electrolyte excretion. Flying as far as Tokyo, the flight crews had no discernible circadian rhythms at all! (Strengers & Esser, 1967).

Japanese investigators recorded the diurnal pattern of body temperature after an east-bound flight that involved a time shift of ten hours. The body temperature disruption took 13 days to reestablish. Maximum temperature shifted towards adaptation by 40 to 50 minutes per day (Sasaki, 1964).

Soviet scientists had perhaps the most flexibility in assessing transmeridian desynchronosis, as there were 11 time zones within what was the USSR! Studying an eight hour flight route from Moscow to Khabarovsk and back to Moscow, researchers found that the crew's relaxation, sleep and feeding schedules were disrupted. These researchers also found changes in visual factors, electroencephalograph and electrocardiograph recordings, and blood pressure (Kravtsov, 1967).

In the United States the Federal Aviation Administration has maintained a research program investigating factors influencing air safety. In a 1965 study of an Oklahoma to Tokyo route, investigators found that rectal temperature adjusted to Tokyo cycles in 3-5 days; where adjustment upon returning to Oklahoma took only one day. Reaction time, decision making, and fatigue all increased with the flight. On an Oklahoma to Manila flight, shifts were noted in body temperature, heart rate, and water loss. Psychological factors such as reaction time and subjective fatigue also increased (although this effect was short lived, with recovery established by the second day in Manila) (Hauty, 1966).

Lynman & Orlady (1980) analyzed 2006 reports of NASAs Aviation Safety Reporting System (ASRS) and found that 21% mentioned factors directly or indirectly related to fatigue. These fatigue-related incidents occurred more frequently between midnight and 0600 hours, and during the approach and landing phases of flight. In 1981, NASA began a program to assess flight crew fatigue in long and short haul operations (Graeber, 1988).

In summary, there appear to be many variables which govern the symptoms an individual experiences with extended air travel. These include time of departure and arrival, length of flight, direction of flight, layovers, travel experience, stress, age, physical condition, food and alcohol consumption, sleep during flight, climate changes, and new social environment.

Time Zones

The earth rotates at a speed of 15 meridians an hour (one meridian every four minutes). The globe is divided into 24 time zones, each corresponding to 15 meridians. When flying in a westward direction, the day lengthens, because the flight counters the earth's rotation (and goes with the relative rotation of the sun), and the clock must be set back as many hours as times zones are traversed. In contrast, eastbound flights counter the relative rotation of the sun, the clock must be set ahead, and the day is "shortened" (Samel & Wegmann, 1989).

Transmeridian Desynchronization

When an individual changes several time zones there is a sudden phase shift of the controlling synchronizers, which usually induces corresponding shifts in circadian rhythms. However, the biological system does not alter immediately; instead, it shows a certain inertia in adjusting to the new local time. The inability of the endogenous rhythm to adjust immediately to an abrupt shift in external zeitgebers causes a transient desynchronization of body and environment.

When an individual flies from one time zone to another, his or her body clock and the rhythms it controls must resynchronize to the local geophysical and social zeitgebers of the destination time zone. Eastern flights shorten the day and require a phase advance, while westward flights lengthen the day and require a phase delay. The impairment of well-being and performance experienced after transmeridian flight is in large part the result of the circadian system's inability to adjust rapidly to sudden shifts in the timing of its zeitgebers. In effect, the system resists changes in its timing and stability. So, resynchronization of the biological timing system can take up to several days (Graeber, 1988).

Even though our myriad circadian rhythms are timed by only one or two clocks, they do not resynchronize together. Different rhythms adjust to the new zeitgebers at different rates, some lagging more than others. "Jet lag" results from external desynchronization (when the timing of their circadian rhythm is not appropriate for local time), and from internal desynchronization (when their readjusting internal rhythms are no longer in phase with each other). A third disruptive aspect to jet lag is the sleep loss that results from the combined influence of both types of desynchronization.

Resynchronization

The number of time zones crossed determines the extent of the phase shift and can also influence the direction of the shift. If fewer than twelve time zones are crossed in the westward direction, resynchronization is accomplished more rapidly by a phase delay similar to the zeitgeber shift. On an eastward flight many travelers' rhythms exhibit a counter intuitive and complementary phase delay after crossing only eight or nine time zones (to the east). Some circadian rhythms adjust by lengthening their periods across 15 hours until they "lock on" destination time (Gander, Myhre, Graeber, Anderson, & Lauber, 1985; Klein & Wegmann, 1980). Some rhythms advance (for example, adrenal hormones), while others, (for example, body temperature), delay to reach the same realignment with the new local zeitgebers. The prolonged phase extension of many

circadian rhythms can probably be attributed to the natural tendency of the biological clock to lengthen its period beyond 24 hours (Wever, 1979).

Most biological rhythms adjust faster after westward flight than after eastward flight (Aschoff, Hoffman, Pohl, & Wever, 1975; Graeber, 1982; Klien & Wegmann, 1980). This asymmetry occurs irrespective of the relative direction of the flight (outgoing or homecoming) or whether the flight takes place during the day or night (Klien, Wegmann, & Hunt, 1972). Neither the time of flight (whether a day or a night flight), nor the relative flight direction (whether outgoing or homecoming), have major influences on the adaptation speed (Klien & Wegmann, 1980). It is argued that because the free-running period for humans is more than 24 hours, the process of adaptation is easier if the phase rhythms are lengthened, as they are after westward flights, rather than shortened, as after eastward flights (Minors & Waterhouse, 1981).

Resynchronization: East versus west

The debate regarding the relative disruption to flying in an easterly or a westerly direction has not been resolved (Seigel et al., 1969). The complexity of the various adjustments to biological rhythms may make such a sweeping judgment difficult. Graeber (1988) maintains there may be two issues involved. One issue involves evaluation of the subjective experience of which direction is easier to travel. A separate but related issue, is which direction is it easier for a traveler's biological rhythms to become entrained.

Sleep and east bound flights

Eastward flights have been found to produce more sleep disruption than westward flights. In a study by Graeber, Dement, Nicholson, Sasaki, & Wegman (1986) sleep quality decreased more after eastward flights than after westward flights. More daytime sleepiness (as assessed by the MSLT) occurs after easterly flights. Sleep after easterly flights is much more variable and fragmented, perhaps because the traveler cannot achieve sleep by conscious effort (Seigel et al., 1969). Sleep patterns are more varied and more fragmented (Nicholson, Pacoe, Spencer, Stone, & Green, 1986; Samel & Wegmann,

1988). When an individual's day is shortened, the traveler typically has decreased total sleep time, decreased sleep efficiency, an increase in slow wave sleep and a decrease in REM (Dement, Seidel, Cohen, Bliwise, & Carskadon, 1986; Sasaki, Kurosaki, Mori, & Endo, 1986).

Sleep and west bound flights

Westbound flights are less disruptive to sleep than easterly flights, which may reflect the greater ease of delaying, rather than advancing, circadian rhythms (Halberg, Nelson, Runge, & Schmitt, 1967). Graeber et al. (1986) notes that after west bound flights the first few nights sleep is usually of good quality and quantity and not unduly disturbed, except more awakenings during the second part of the night. When traveling West, sleep onset typically occurs earlier as a consequence of sleep deprivation that results from a delay shift (Nicholson et al., 1986: Wegmann et al., 1986). After westbound flights the typical night EEG shows decreased sleep time, decreased sleep efficiency, increased slow wave sleep, and no apparent disruption of REM (Dement et al., 1986; Nicholson et al., 1986). The amount of time flight crews spent in bed decreased after west flights. After homeward flights, sleep appears to increase (Suvantao, Partinen, Härma, & Ilmarinen, 1990).

Flight Related Sleep Problems

Transmeridian flight leads to irregular sleep (Nicholson, 1972). Disturbance of normal sleep patterns is the most common physiological symptom associated with long-haul flying. The quality of sleep, perceived adjustment, and recovery times depend on the flight direction and on the number of time zones crossed after transmeridian flights. Most of the sleep deficit on trips results from later sleep onset times, not advanced to compensate for earlier awakenings at home. Travelers have difficulty adjusting their sleep habits to get home-equivalent sleep.

Sleep is often disturbed because it is attempted during an inappropriate phase of the circadian system, or at periods when the local environmental conditions are disadvantageous. The timing of the trips, as well as the length of the flight, may contribute

to fatigue. In addition, the regular cues for sleep are not necessarily found at the destination. Travelers may stay up later on trips, as they are no longer under the social control of the home and family environment. Conversely, travelers may not retire to bed early enough to compensate for early morning flights as they are under the social control of the home and family environment. Flight attendants sleep longer at home than abroad, regardless of flight direction (Suvanto, Partinen, Härmä, & Ilmarinen, 1987).

Short and Long Haul Effects

Short-haul flights, that travel no more than one time zone are, in general, safer than long haul flights that traverse multiple time zones. This is despite the fact that short and medium range jet aircraft performed 3.34 times more landings and takeoffs than long range aircraft. There is little doubt that the impact of time zone changes on crew performance is a significant factor behind the higher accident rate for long-haul flights (Caesar, 1986). Short haul flights are not associated with sleep or mood disturbance, however, Klien, Bruner, Kuklinski, Ruff, & Wegmann (1972) suggest that even short-haul crews have compromised performance because their work, at times, is in conflict with their circadian rhythms. The consequences of short-haul flights appear more of a matter of personal comfort and health.

Individual Differences & Resynchronization

Substance use and resynchronization

Stimulants have been used to counter the effects of fatigue with extended flights, or routes of multiple short-haul flights. The use of caffeine and tobacco for combating fatigue is legendary among flight crews (McFarland, 1941). Graeber (1988) found that pilots consume significantly greater caffeinated drinks during trips than at home and the average daily intake of caffeine increased each day on an extended trip, reaching the highest levels during the last day. Pilots that smoked increased smoking gradually, so the average increment increased over 50% over 4 days. The use of alcohol by flight crews was significantly more on trips than at home. While alcohol use may be used as an aid for

relaxation and inducing sleep, it disturbs REM sleep and is detrimental to sleep quality (Knowles, Laverty, & Kuechler, 1968).

Age and resynchronization

Age has been associated with a number of sleep parameters including total sleep time, duration of slow wave sleep (Sasaki et al., 1986), duration of time in bed, sleep latency, and complaints of awakening (Miles & Dement, 1980). Older flight crew members, especially those over 50, have reported less total sleep, as well as poorer sleep quality than their younger peers (Dement et al., 1986; Nicholson et al., 1986; Preston, 1973). Older pilots perceived their sleep quality and adaptation as poorer, and they had longer recovery times than younger subjects. Age explained some variation of perceived desynchronosis in flight attendants (Suvanto et al., 1987).

Morning types and evening types

Adjustment to transmeridian flight may be influenced by the nature of the traveler's regular activity-sleep schedule. It may make a difference if the traveler is an early or a late riser (Seigel et al., 1969). These differences in type can be reliably differentiated on the basis of subjective alertness, daytime EEG, and body temperature (a later temperature peak is typical of a late sleeper) (Miles & Dement, 1980).

These circadian tendencies may mask some of the time shift effect because they influence the time of maximal sleepiness (Sasaki, et al., 1986). However, studies have not strongly supported that 'morningness' and 'eveningness' were related to desynchronization. Logically, morning types would adapt themselves better to the phase advances of eastward flights, and evening types would adapt best to the phase delays of night work and westward flights. However, results have not supported this hypothesis (Miles & Dement, 1980).

Treatment of Desynchronosis

If desynchronosis, with its associated disruption of sleep and other physiological systems, promotes an increase in seizures for those with epilepsy, then approaches to

minimizing the effects of desynchrony may not only reduce the discomfort of "jet lag" but may also prevent a lowering of the seizure threshold. Self-help books, research articles, and common lore abound with remedies for the disruption of extended flight (for example, Ehret & Scanlan, 1983). Most "jet-lag" remedies focus on ways to reduce sleep disruption; many also recommend changes in diet and exercise. Seigel et al. (1969) propose four strategies. First, adjusting clock time and the environmental factors (for example, room light) to be in synchrony with those at the point of origin. Wiley Post, before his historic flight around the world, adjusted his day-night activity cycle to match a mid-point on his flight (Post & Gatty, 1931). Second, schedule flight time that is least disruptive to preflight circadian rhythms. According to the International Civil Aviation formula (Seigel et al., 1969) departures between 0800—1200, and arrivals between 1800—2200 are least disruptive. Third, pace activities during the initial period of rephrasing so superimposed stresses are kept to a minimum, especially heavy eating and drinking. Finally, avoid taking hypnotics, with their consequent loss of REM sleep.

Studies of flight crew behavior show that most subjects were able to get adequate sleep during the layover either by sleeping efficiently at selected times, or by sleeping less efficiently but staying in bed longer than usual. Eastward flying crews could largely improve their chance of getting good layover sleep by adhering to a more-structured sleep schedule (Graeber, Lauber, Connell, & Gander, 1986). Graeber and colleagues recommend that crews limit their sleep immediately after arrival, and prolong the subsequent wakeful period to end about the normal local time for sleep. Proper sleep scheduling during the first 24 hours of the layover is particularly critical. Also, limited naps can be a helpful strategy to improve alertness (Mullaney, Kripke, Fleck, & Johnson, 1983; Nicholson, Pascoe, Roehrs, Roth, Spencer, & Zorick, 1985). Stimulating activity for pilots who fly long, boring flights, particularly those over water has been suggested. Creating an atmosphere opposite to the MSLT would reduce the amount of sleepiness experienced in a soporific environment (Graeber, 1988).

Desynchronosis and Seizures

As previously suggested, if desynchronosis from air travel leads to sleep disruption and sleep loss than it may well contribute to an increase in seizures; circadian rhythm disruption may correlate with post-flight seizure frequency. Several factors may contribute to an increase in desynchronization including, flight direction, length of flight, travel time, and the time of departure and arrival (Seigel et al., 1969). Health status and behavioral factors, such as diet, exercise, and substance use may moderate or exacerbate the circadian rhythm disruption that results from air travel (Ehret & Scanlan, 1983). Investigating factors associated with biological rhythm disruption from flight may aid in understanding the relationship between air travel and seizures and may even be useful in identifying risk factors for post-flight seizure increase.

Hypotheses and Expected Findings

As an unprecedented investigation, this research is clearly exploratory. However, as noted by Tukey (1977) exploratory studies need not be limited to description—exploratory and confirmatory investigation can, and should proceed side by side. In this light, the following exploratory hypotheses were investigated.

Hypothesis 1: Air travel is associated with a non-random pattern of seizure occurrence, specifically that seizures are more prevalent during the week after flying than for the week prior to air travel.

Hypothesis 2: Sleep loss is associated with an increase in post-flight seizure frequency.

Hypothesis 3: Sleep is increasingly variable around periods of air travel which is associated with an increase in post-flight seizure frequency.

Hypothesis 4: Measures of circadian rhythm disruption are positively correlated with post-flight seizure increase.

Hypothesis 5: Baseline seizure frequency is positively associated with post-flight seizure increase.

Chapter II

METHOD

Recruitment

The low prevalence of epilepsy in the general population and the infrequency that most individuals travel by air, (which may be particularly infrequent for individuals with epilepsy), required that recruitment be extensive. Recruitment occurred throughout a three year period from 1990 to 1993. Subjects were recruited through neurologists offices, non-profit epilepsy organizations, and through direct solicitation through the mass media (newspaper and radio). Neurologists in Hawaii, Rhode Island, and Badden Vertemburg (Germany) encouraged their patients with epilepsy to participate in the study. Subjects were also recruited through local chapters of the Epilepsy Foundation of America (EFA) and at three national conferences of the EFA. Recruitment was also done by announcements in newspaper articles and radio announcements.

Procedure

Subjects responded to mass media announcements that a study was being conducted to investigate how air travel effects individuals with epilepsy. Subjects telephoned or wrote to the author directly, or called or wrote to their local chapter of the Epilepsy Foundation of America. Subjects were then informed about the requirements of participation, such as completing a questionnaire and monitoring their sleep and seizure for a 15 day period. An informed consent statement was not considered necessary as the risk involved in completing a questionnaire and self-monitoring was negligible. Subjects were told that their participation would be confidential and that they need not include their names on the questionnaire. Once a potential subject agreed to participate they were sent a questionnaire entitled the Epilepsy and Air Travel Questionnaire (EATQ) (see Appendix A) with a return addressed envelope.

Seven days prior to their next flight subjects began monitoring their sleep and seizures. Subjects continued this monitoring for 15 consecutive days. Subjects also

completed questions regarding their epilepsy, health habits, and previous experience with air travel; completing this section of the questionnaire could be done at any time. During or soon after their flight subjects were asked to complete a section of the questionnaire that addressed their flight, as well as their behavior during the flight. After the last day of monitoring subjects mailed the questionnaire to the author.

Subjects recruited from neurologists offices followed a similar procedure. Once identified by the neurologist or the neurologists staff as an individual with epilepsy, the patient was asked if he or she were intending to travel by air in the next few months. If the patient was planning to travel by air he or she was then asked if they were interested in participating in a study of epilepsy and air travel. If the subject expressed an interest in participating they were given a packet containing a cover letter (see Appendix B), the EATQ, and a return addressed envelope.

On occasion parents of children with epilepsy were interested in having their child participate in the study. There were no restrictions on having children participate so long as a parent was willing to complete the questionnaire and monitor the child. Parents were encouraged (by letter or phone conversation) to be equally vigilant for seizures during the week prior to air travel as during the post-flight week. Parents were also encouraged to ask their child on a daily basis about having seizures.

Subject Criteria

Subjects were encouraged to participate if they had epilepsy and were planning to travel by air. Subjects must have been able to provide prospective data as previously described. No restrictions were made as to demographics, extent of air travel, or type of epilepsy. Child subjects were accepted if the subject's parent or guardian was prepared to assist with the completion of the questionnaire and monitor the child's sleep and seizures.

Subjects

Forty-five subjects returned questionnaires. Three of these questionnaires were not included because they were completed retrospectively and four questionnaires were not

included because respondents did not document having taken a flight. A single questionnaire was not able to be included as the respondent failed to monitor the post-flight week.

Of the 37 subjects that participated as intended, most were female, between 30 and 40 years of age, Caucasian, well educated and employed (see Table 1).

Most subjects had generalized seizures or both generalized and partial seizures. About half of the subjects reported experiencing auras. Almost all subjects reported currently taking anti-seizure medications and most subjects had good control over their seizures; over half of the subjects reported having fewer than one seizure per month prior to involvement with the study and the modal frequency of monthly seizures was zero. Most subjects reported that being short on sleep was a trigger for their seizures (see Table 2).

Most subjects were familiar with air travel prior to involvement with the study. Ten subjects reported having taken more than 100 flights, the mean number of flights taken since developing epilepsy was 82, and only six subjects had taken less than 10 flights. Twenty-five subjects reported flying in the past year with an average of eight flights taken during that year. Almost one-third of participants stated a fear of having a seizure while flying, while only four indicated that they actively avoided flying. Sixteen subjects reported having an increase in seizures after flights taken prior to involvement with this study (see Table 3).

Table 1.
Subject Demographic Characteristics

	Number of Subjects
Recruitment	
Public Announcement	17 (46%)
Epilepsy Foundation of America	14 (38%)
Neurologists Office	3 (8%)
Germany Epilepsy Centers	2 (5%)
Hospital Referral	1 (3%)
Sex	
Male	11 (30%)
Female	26 (70%)
Ethnicity	
Caucasian	33 (89%)
Japanese-American	4 (11%)
Marital Status	
Single	14 (38%)
Married	20 (54%)
Widowed/Divorced	3 (8%)
Employment	
Full-Time	23 (62%)
Part-Time	2 (5%)
Students	4 (11%)
Homemakers	4 (11%)
Retired	2 (5%)
Unemployed	1 (3%)
Education*	
High school	5 (14%)
College	18 (49%)
Graduate/Post College	12 (32%)
Age Mean = 38.70 SD = 12.62	Range 9—70

* One 9 year old subject had an age-appropriate 4 years of education.

Table 2.
Subjects' Epilepsy Characteristics

		Number of Subjects
Seizure Type	Generalized Only	17 (46%)
	Partial Only	3 (8%)
	Generalized & Partial	13 (35%)
	Auras	18 (49%)
Anticonvulsant Use	No Anticonvulsant	2 (5%)
	Single Anticonvulsant	21 (57%)
	Two Anticonvulsants	12 (32%)
	Three Anticonvulsants	1 (3%)
	Four Anticonvulsants	1 (3%)
Age at First Seizure	Birth/Infancy (0—2 years)	6 (16%)
	Childhood (2—11 years)	9 (24%)
	Adolescence (12-18 years)	5 (14%)
	Early Adulthood (19—25 years)	7 (19%)
	Middle Adulthood (26—50 years)	7 (19%)
	Late Adulthood (51 & above)	2 (5%)
	Mean Age at First Seizure = 18 (15)	
Seizures per Month	Less than 1	21 (57%)
	1 to 1.9	5 (14%)
	2 to 3.9	2 (5%)
	4 to 7.9	4 (11%)
	8 to 12	3 (8%)
	1 outlier of 55 seizures per month	
	Mean Seizure Rate Per Month (without outlier) = 1.77 (2.80)	
Seizure Triggers	Low on Sleep	28 (76%)
	Psychological Stress	26 (70%)
	Physical Stress	14 (38%)
	Skipping Meals	11 (30%)
	Change in Medication	7 (19%)
	Alcohol Use	7 (19%)
	Menstruation	7/26 (27% of women)
	Pain	2 (5%)

Table 3
Subject's Flight History

	All Subjects	Subjects without Seizure Increase	Subjects with Seizure Increase
Flights last month			
Mean	1.68	1.5	2.22[a]
SD	3.57	4.0	1.64
Mode	0	0	4
Minimum	0	0	0
Maximum	21	21	4
Flights last year			
Mean	8.47	9.07	6.67
SD	11.47	12.83	5.94
Mode	2	1	2
Minimum	0	0	0
Maximum	60	60	18
Flights taken since first seizure[b]			
Mean	81.57	92.19	50.89
SD	176.7	203.43	43.54
Mode	100	—	1000
Minimum	0	1	0
Maximum	1000	1000	116
No. times seizures post-flight			
Mean	4.06	1.68	12.57
SD	11.92	3.21	24.19
Mode	0	0	2
Minimum	0	0	1
Maximum	67	12	67
Avoid flying?			
Yes	4 (11%)	1 (4%)	3 (33%)
No	33 (89%)	27 (96%)	6 (66%)
Worried about seizure on flight?			
Yes	11 (30%)	4 (14.2%)	2 (22%)
No	26 (70%)	24 (86%)	7 (78%)

[a] Subjects with post-flight seizure increase flew more frequently for the month prior to involvement with the study. df = 8, 2 tailed t =-.2.63, p =.03

[b] Subjects were requested to report the approximate number of flights (to the nearest 100) if over 100 flights were taken since first experiencing seizures.

Measures

Epilepsy and Air Travel Questionnaire (EATQ)

Subjects completed a questionnaire and self-monitoring schedule, the EATQ (see Appendix A). A German version of the questionnaire was also developed (Appendix C) and the back-translation was done to verify equivalence (Appendix D). Completed EATQs were considered for analysis if a flight was taken and the data were reported prospectively. The EATQ was constructed by the author and consisted of four sections. The first section included questions developed by the author, addressing the subject's demographics, epilepsy, sleep habits, substance use, and prior experiences with air travel. Subjects were also asked to report their medication use.

Section 3 contained questions, developed by the author, about the subject's flight and behavior while flying. This section was to be completed as soon as possible after the flight is taken. Subjects were asked about their medication and substance use during their air travel. The selection of questions in Section 3 was also guided by information required to establish the ICAO formula for circadian rhythm disruption (see below).

Monitoring of sleep and seizures

Section 2 and 4 were monitoring schedules, designed by the author, that required the subject (or the subject's parent or guardian) to record the number of seizures per hour on a daily basis for the week before and the week after their flight. Daily diaries are used widely in neurological research and clinical practice to assess alterations in seizure frequency among patients with epilepsy. Groh, Tatzer, & Schubert (1987) found that the daily dairy is a reliable method for securing data on seizure counts. Similarly, sleep diaries have been widely used in sleep research, typically with patient's complaining of sleep disorders (Hauri, 1982) The period of one week before and after flying was chosen as studies of extended flight indicate physiological and subjective sleep parameters can take

several days to approach baseline (for example, Buck, Tobler, & Borbely, 1989). Extending the self-monitoring task beyond one week may have also reduced compliance.

Subjects (or the subject's parent or guardian) monitored their sleep for the week before and the week after their flight. They indicated when they slept by drawing a line on the monitoring schedule (see Appendix A). This method, suggested by Graeber (C. Graeber, personal communication, May 26, 1991), is believed to accurately reflect total sleep times as well as indicate when the subjects slept.

Variables Defined

Seizure Frequency and Post-Flight Seizure Increase

Subjects (or the subject's parent or guardian) reported seizure frequency (per hour) on the schedule provided. No request was made to evaluate the severity or type of seizure. Aura's that were not immediately followed by a seizure were considered as seizures. Post-flight seizure increase was determined by subtracting the mean pre-flight daily seizure frequency from the mean of post-flight daily seizure frequency.

Sleep Loss

Total sleep time (TST) was measured by the hours of sleep indicated by subjects per 24 hour periods. Sleep loss was computed by subtracting the mean TST for the week after air travel from the week before air travel. Sleep loss was also determined by a daily comparison of TST.

Sleep Variability

Sleep variability was measured by the standard deviation of sleep for all subjects in a given 24 hour period. Individual sleep variability was also computed by determining the standard deviation of TST for days before and after flying. No request was made of subjects to rate the quality of sleep.

Circadian Rhythm Disruption

Circadian rhythm disruption was assessed using a formula developed by the ICAO (Seigel, Gerathewohl, & Mohler, 1969). This formula has been used to determine the

amount of rest time required for a flight crew who have previously flown an extended flight. The formula considers travel time, time zones traveled, and departure and arrival times in determining the amount of rest time required (see Figure 1). The components of this measure will also be considered individually as measures reflecting circadian rhythm disruption.

$$\text{Circadian Rhythm Disruption} = \frac{\text{Travel Time (Hours)}}{2} + \text{Time Zones (in excess of 4)} + \text{Departure Time Coefficient} + \text{Arrival Time Coefficient}$$

Departure and arrival time coefficients used in the ICAO formula

Period	Departure Time Coefficient	Arrival Time Coefficient
0800—1159 hours	0	4
1200—1759 hours	1	2
1800—2159 hours	3	0
2200—0059 hours	4	1
0100—0759 hours	3	3

Figure 1: International Civil Aviation Organization measure for circadian rhythm disruption

Baseline Seizure Frequency

Baseline seizure frequency will be provided by subjects completing the EATQ (see Appendix A, question number 14). Subjects responded to a question asking them to record the average number of seizures they have experienced per month for the 12 months preceding their involvement in the study.

Statistical Analysis

Data from 37 EATQs were entered into an Apple Macintosh IIsi computer, using STATVIEW statistical analysis software (Haycock, Roth, Gagnon, Finzer, & Soper, 1992) See Appendix E for a compilation of the entire data set.

The distributions of main variables were plotted to assess for normality of distribution. When skew and kurtosis were significant several data transformations were tried to render these distributions normal, such as a square root transformation, a logarithm transformation and an inverse transformation. A correlation matrix was computed of main variables (and main variables that required transformation) (see Table 4).

Descriptive statistics (such as, category, mean, mode, standard deviation, minimum and maximum scores) were determined for subject demographics, flight history, air travel, seizure, sleep, and circadian rhythm variables. Pre- and post-flight sleep comparisons, as well as day by day comparisons regarding sleep, were made using Student's t-test. Comparisons between subjects with post-flight seizure increase and those without post-flight seizure increase were also computed using Student's t-test. A Chi Square analysis was used to determine the significance of expected to actual post-flight seizure rate. Finally, simple regression analysis was used to determine the significance of predictors of post-flight seizure increase.

Chapter III.

RESULTS

A correlation matrix of basic demographic and epilepsy variables, and variables central to the evaluation of the hypotheses was computed (see Table 4). With one exception, demographic variables, such as sex and age did not correlate significantly with variables considered in the evaluation of hypotheses. Age was negatively correlated with seizure frequency per month (r=-.40). This significant correlation was largely influenced by the youngest subject (9 years of age) having a very high monthly seizure frequency (55 seizures per month). Seizure types, such as generalized and partial seizures, did not appear to relate meaningfully to those variables considered in the evaluation of hypotheses. Partial seizures correlated with pre-post sleep net change (-.48), ICAO score (-.34), and seizures per month after transformation (.46). The correlation of those variables considered in the evaluation of the hypotheses will be addressed below.

Air Travel

A total of 58 flights were taken—14 subjects had connecting flights. The mean duration of total flight time was 360 minutes (six hours) with a standard deviation of 266 minutes. The mean distance was 2413 miles with a standard deviation of 2093 miles (see Table 5). Eight flights involved international travel. Fourteen flights were in a mostly easterly direction, 15 flights were in a mostly westerly direction, and 10 flights were mostly north-south (see Figures 2-3). Twenty-eight flights crossed one or more time-zones, with a mean crossing of 2.8 time zones. Approximately half of the flights departed and arrived during the morning hours, from 8 a.m. to noon (local time).

Table 4
Correlation of Main Variables

	Sex	Age	General Seizure	Partial Seizure	Seizure/ Month	Trans. Sz Month[a]	Travel Time
Sex							
Age	-.23						
Genrl Sz	-.09	-.06					
Partial Sz	.03	.03	-.07				
Sz/Month	-.21	-.40*	-.01	-.25			
Trans. Sz Month	.04	. 26	-. 26	. 46**	-.53**		
TravTime	.12	.12	-.16	-.20	-.11	-.21	
Tm-Zone	.21	.09	-.08	-.26	-.16	-.08	.82**
CRD	.14	-.02	-.03	-.34	.15	-.29	.61**
Direction	-.30	-.07	.03	.17	.30	-.12	-.16
Distance	.21	.06	-.05	-.15	-.09	-.21	.92**
Sleep Loss	-.19	.13	-.03	-.48**	.15	-.05	.05
M Sz Diff	-.05	-.32	-.10	-.15	.38*	-.43**	.17
Trans. M Sz Diff[b]	.04	.19	-.04	.10	-.34**	.38**	-.09

	Tm-Zone	CRD	Direction	Distance	Sleep Loss	M Sz. Diff.	Trans. M Sz Diff
Tm-Zone							
CRD	.67**						
Direction	-.29	-.11					
Distance	.90**	.63**	-.15				
Sleep Loss	.24	.12	.05	.14			
M Sz Dif	.16	.16	.13	.21	.04		
Trans. M Sz Diff	-.08	-.11	-.09	-.15	.05	-.73**	

Note. N of correlations was 36 or 37 for all variables except Sleep Loss which was 33.

* $p < .05$
** $p < .01$

Table 5
Air Travel

	All Flights (n=37)	East Flights (n=14)	West Flights (n=15)	North/South Flights (n=8)
Distance (miles)				
Mean	2413	2539	2759	1542
SD	2093	1841	2547	1452
Minimum	136	169	136	496
Maximum	9476	5472	9746	4839
Time-Zones				
Mean	2.81	3.21	3.55	.75
SD	2.77	2.42	3.27	.50
Minimum	0	0	0	0
Maximum	11	9	11	2
Travel Time (minutes)				
Mean	360	360	403	247
SD	266	266	338	226
Minimum	60	65	60	90
Maximum	1440	660	1440	780

Note. The number of flights does not include connecting flights

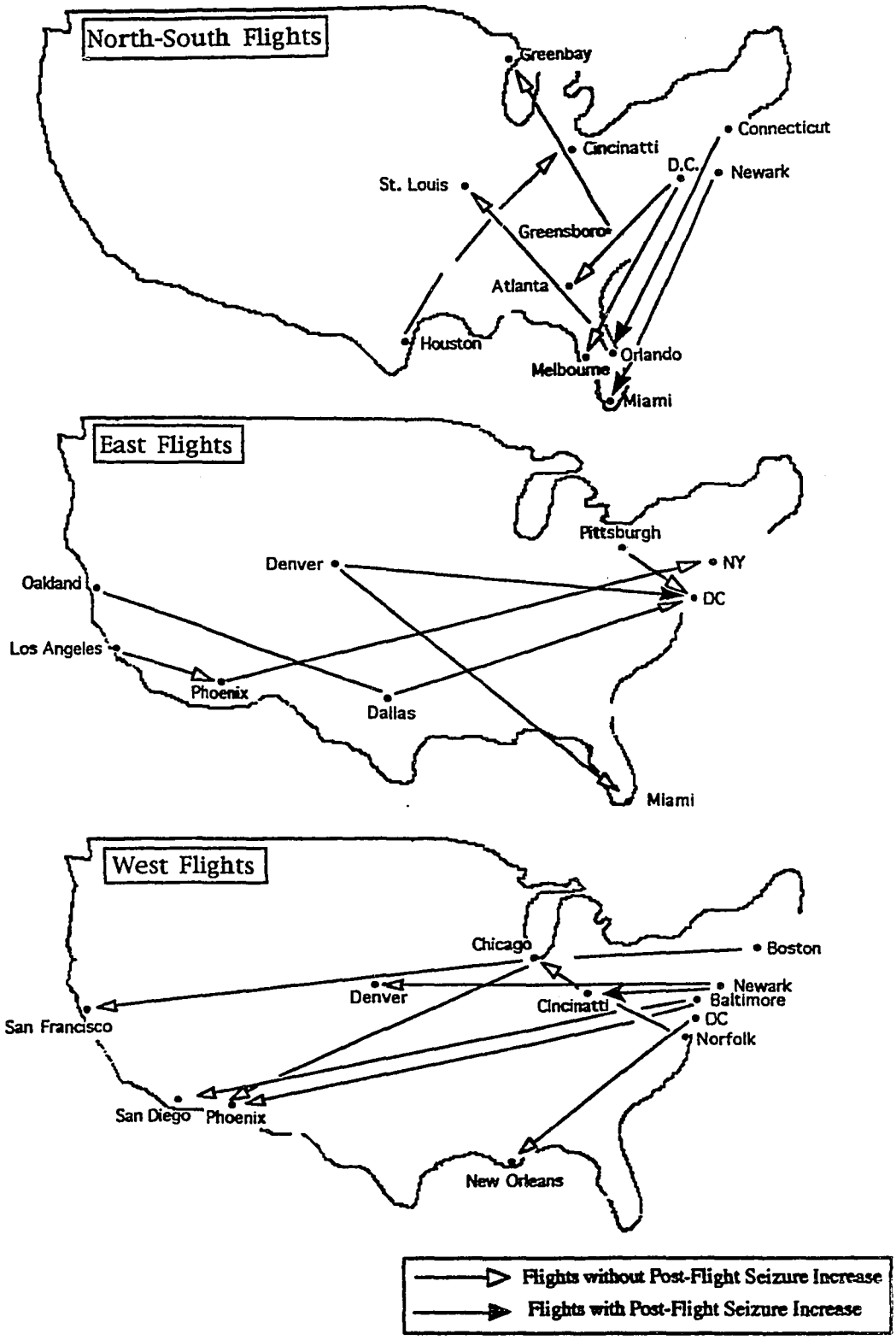

Figure 2: Subjects' Air Travel in the Continental U.S.A.

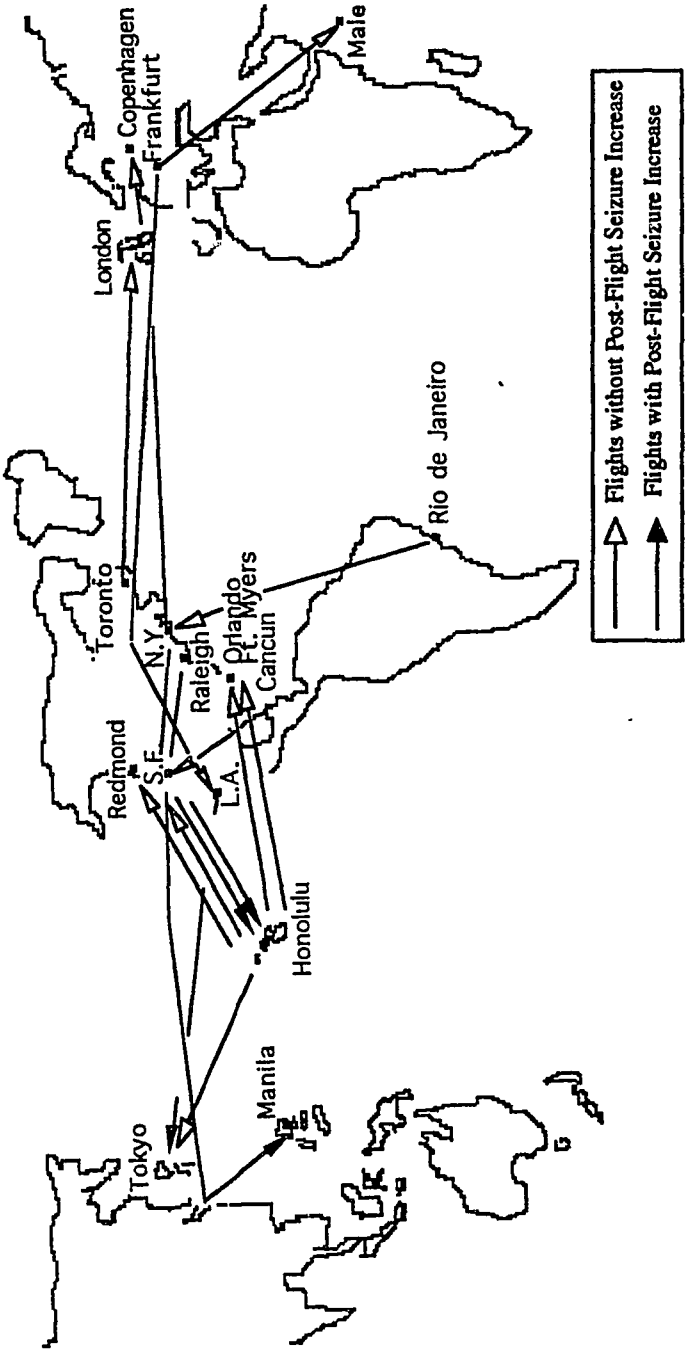

Figure 3: Subjects' International and Overseas Air Travel

Hypothesis 1: Pre-Post Seizure Frequency

Twenty-three out of the 37 subjects did not have seizures before or after flying. Of the remaining 14 subjects, 9 had more seizures after flying, 2 had the same number of seizures, and 3 had a decrease in post-flight seizure frequency. (It should be noted that one of the three subjects who reported a decrease in seizures after flying significantly increased the dosage of her anticonvulsant medication for the post-flight week.) The mean number of seizures per day for the week prior to flying was 4.75; this rate increased significantly to 8.75 seizures per day for the week after flying (see Table 6). For those who experienced post-flight seizure increase the mean seizure rate prior to and after flying was 2.71 and 11.62 respectively. Four subject's post-flight seizure increases were particularly striking with increases of 13, 16, 18 and 30 seizures. Three of the nine subjects who experienced post-flight seizure increase reported most frequently having generalized seizures, four subjects had both generalized and partial seizures, one subject reported having only partial seizures, and one subject reported having only absence seizures.

Hypothesis 2: Sleep Loss and Post-Flight Seizure Increase

There was a significant decrease in TST for the day prior to air travel (see Table 9). Subjects with seizure increase reported a significant decrease in TST for the first four days after air travel compared to their TST for the pre-flight week. Surprisingly, sleep loss did not significantly correlate with post-flight seizure increase or post-flight seizure increase after transformation.

Table 6
Seizures Pre and Post-Flight

	Pre-Flight (7 days)	Post-Flight (8 days)
No. Subjects with Seizures	8	12
Mean Seizures per Day	4.75	8.75*
SD Seizures per Day	2.46	6.82
Modal Seizures per Subject per Day	0	0
Max.Seizures per Subject per Day	12	32

* $p < .01$ (Chi Square = 136.91)

Table 7
Seizures by Day

Day	Total Number of Seizures	Number of Subjects with Seizures	Mean Seizures per Subject
1	11	5	2.2
2	5	3	1.6
3	3	2	1.5
4	2	2	1
5	6	5	1.2
6	6	4	1.5
7	6	4	1.5
8	22	5	4.4
9	7	5	1.4
10	17	3	5.6
11	26	6	4.3
12	8	4	2
13	9	5	1.8
14	6	2	3
15	10	4	2.5

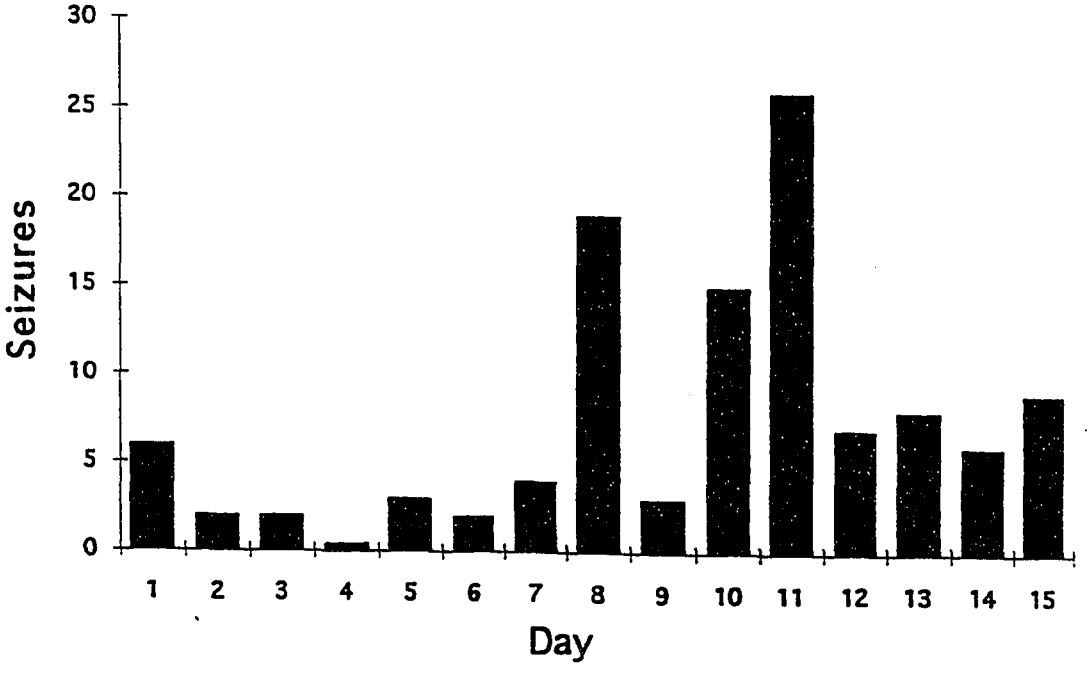

Figure 4: Sum of Seizures by Day

Table 8
Sleep— Pre-and-Post-Flight

	Pre-flight (7 days)	Post-flight (8 days)	Loss/ Gain	Significance (2 tail t-tests)
All Subjects (n=33[a])				
Mean TST[b]	7.66	7.99	+ .33	df=6, t=-.46, p=.65
SD of TST	1.30	1.88	+ .58	df=6, t=-.47, p=.19
Subjects without seizure increase (n=26)				
Mean TST	7.35	7.61	+ .26	df=6, t=.85, p=.42
SD of TST	.55	.57	+.02	df=6, t=1.03, p=.34
Subjects with Seizure Increase (n=7)				
Mean TST	7.58	7.08	-.50	df=6, t=1.54, p=.17
SD of TST	.54	.48	-.06	df=6, t=1.76, p=.12

Note. t-tests compared 7 days before flight and 7 days after flight (omitting day 15)
[a] Four subjects failed to provide complete sleep data.
[b] TST values represent hours in a 24 hour period.

Hypothesis 3: Sleep Variability and Post-Flight Seizure Increase

Sleep variability (standard deviation of TST) significantly increased for the day prior to air travel and the day of the flight (see Table 9). Sleep variability was not significantly greater for those with post-flight seizure increase (see Table 8). Three of the nine subjects who experienced post-flight seizure increase actually experienced a decrease in sleep variability during the post-flight week.

Hypothesis 4: Circadian Rhythm Disruption and Post-Flight Seizure Increase

The mean ICAO score for circadian rhythm disruption for all subjects was 6.68 (standard deviation = 3.64). This equates to a rest period of 16 hours that would be required of flight crews prior to their next flight (given ICAO guidelines). The modal ICAO score was 4.62, which equates to a rest period of approximately 11 hours (see Table 10).

Other measures reflecting circadian rhythm disruption, indicated that the average flight crossed approximately three time-zones, flew over two thousand miles, and lasted for approximately six hours.

Mean measures of time-zones crossed, distance, and travel time was greater for subjects with post-flight seizure increase compared with those without seizure increase. Distance traveled for those with post-flight seizure increase was significantly greater than subjects who did not experience such an increase in seizures (see Table 10).

Table 9
Sleep Time by Day

Day	All Subjects (n=33) TST	SD	Subjects without Seizure Increase (n=26) TST	SD	Subjects with Seizure Increase (n=7) TST	SD
1	7.67	(1.31)	7.62	(1.36)	7.86	(1.18)
2	7.66	(1.51)	7.62	(1.51)	7.81	(1.69)
3	7.56	(1.49)	7.60	(1.62)	7.44	(1.05)
4	7.71	(1.70)	7.55	(1.79)	8.25	(1.36)
5	7.36	(1.54)	7.27	(1.60)	7.62	(1.41)
6	7.34	(1.62)	7.25	(1.74)	7.62	(1.19)
7	6.24 **	(2.49) **	6.15 **	(2.65) **	6.50	(1.98)
8	6.37	(2.83) **	6.42	(2.68) **	6.18	(3.56) **
9	7.99 **	(1.88)	8.27 *	(1.94)	7.06	(1.40)
10	7.70	(1.83)	7.83	(1.86)	7.25	(1.77)
11	7.46	(1.86)	7.59	(1.78)	6.93	(2.21)
12	7.79	(1.81)	7.81	(1.91)	7.75	(1.56)
13	7.66	(2.29)	7.81	(2.39)	7.12	(1.96)
14	7.52	(1.67)	7.58	(1.70)	7.32	(1.69)
15	7.26	(1.84)	7.13	(1.94)	7.71	(1.47)

* Significant difference from previous days' scores, 2 tailed t, $p < .05$
** Significant difference from previous days' scores, 2 tailed t, $p < .01$

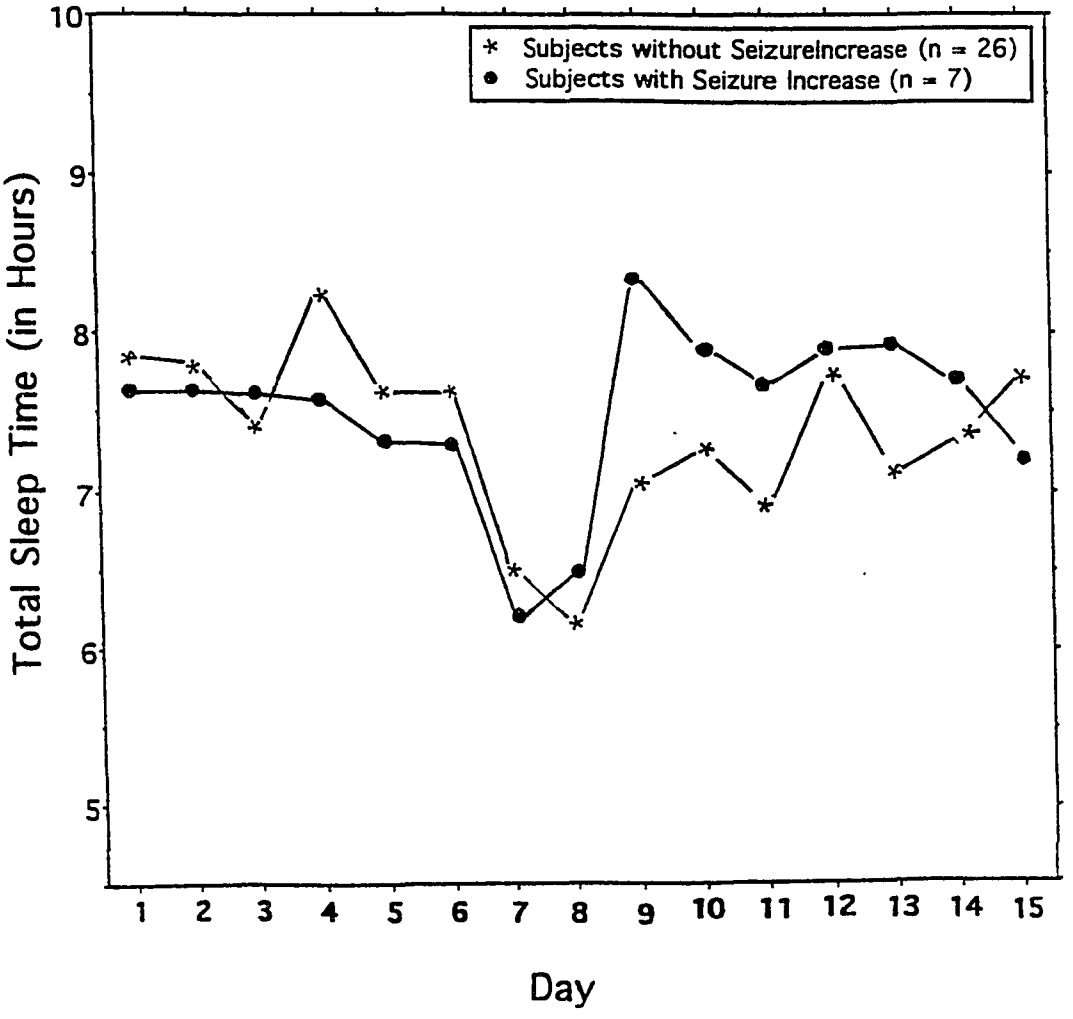

Figure 5: Total Sleep Time by Day

Table 10
Circadian Rhythm Disruption

	All Subjects (n=37)	Subjects without Seizure Increase (n=28)	Subjects with Seizure Increase (n=9)
ICAO Formula[a]			
Mean	6.68	6.63	6.85
SD	3.64	3.66	3.82
Minimum	1.37	1.37	3.00
Maximum	15.25	15.25	14.00
Travel Time (hours)			
Mean	360	312	507
SD	266	194	400
Minimum	60	60	120
Maximum	1440	780	1440
Time-Zones			
Mean	2.81	2.57	3.56
SD	2.77	2.53	3.47
Minimum	0	0	0
Maximum	11	9	11
Distance (miles)			
Mean	2413	2103	3376[b]
SD	2093	1736	2856
Minimum	136	136	1019
Maximum	9746	5796	9746

[a] ICAO formula is reported in Figure 1

[b] Significantly greater distance traveled by subjects with post-flight seizure increase 2-tailed t=-2.35, df=8, p=.04

Despite the significant finding above, distance traveled failed to correlate significantly with an increase in post-flight seizures (either before or after attempts to normalize the distribution of post-flight seizure increase)(see Table 4). These low correlations are believed to have resulted from the skew of post-flight seizure increase (even after transformation the skew of post-flight seizure increase was 1.5) and not represent a lack of relatedness. Surprisingly, there were no significant correlation between ICAO score, distance traveled, travel time, and time-zones traveled, and sleep loss or sleep disruption.

Hypothesis 5: Baseline Seizure Frequency and Post-Flight Seizure Increase

Baseline seizure frequency was significantly associated with post-flight seizure increase. The mean baseline rate of seizures for those who experienced post-flight seizure increase was significantly higher than those subjects who had no post-flight seizure increase (see Table 11).

The rate of seizures per month correlated with post-flight seizure increase ($r=.38$). As previously noted, the distributions of baseline seizure frequency and post-flight seizure increase were positively skew (5.00 and 3.51 respectively). The skew of these distributions were largely contributed to by a modal seizure frequency of zero seizures per month and a modal seizure increase of zero. As both distributions were skew in the same direction the correlation may well represent their "true" relatedness. To test this consideration both distributions were transformed to best approximate a normal distribution. In this case, both variables were best normalized by adding a constant of 1 and inverting the sum. The skew of baseline seizure frequency and post-flight seizure increase was reduced to .32 and 1.6 respectively. The correlation of these transformed variables was .38 (see table 4) indicating that the untransformed variables when correlated is likely to be an accurate representation of their degree of relatedness. As such, a simple regression analysis was chosen to test the significance of baseline seizure frequency as a predictor of post-flight seizure increase. As noted in Table 12 and Figure 3, baseline seizure frequency was a significant predictor of post-flight seizure increase at a $p<.05$ level.

Summary of Results

In sum, three of the five exploratory hypotheses were supported by this study. Seizures appear to occur non-randomly, predominantly after air travel. Measures of circadian rhythm disruption, particularly travel time and distance are positively correlated with post-flight seizure increase. Baseline seizure frequency, or the "control" an individual with epilepsy has over his or her seizures is predictive of an increase in seizures after flying. Surprisingly, sleep variables appear to have little relationship to either measures of circadian rhythm disruption or an increase in seizures after flying.

Table 11
Baseline Seizure Frequency

	All Subjects (N=35)	Subjects without Seizure Increase (N=27)	Subjects with Seizure Increase (N=8[a])
Mean	1.77	1.33	3.25[b]
SD	2.81	2.35	3.81
Mode	0	0	.5
Minimum	0	0	.5
Maximum	11	8	11

[a] Outlier of 55 seizures per month is removed

[b] Subject with post flight seizure increase have significantly greater baseline seizure frequency. df =7, 2 tailed t=2.28, p =.05

Table 12
Simple Regression: Baseline Seizure Frequency and Post-Flight Seizure Increase

Count	R	R-Squared
36	.38	.14

Analysis of Variance Table

Source	DF:	Sum Squares	Mean Square	F-Test
Regression	1	2.82	2.82	5.79
Residual	34	16.56	.49	p=.02
Total	35	19.38		

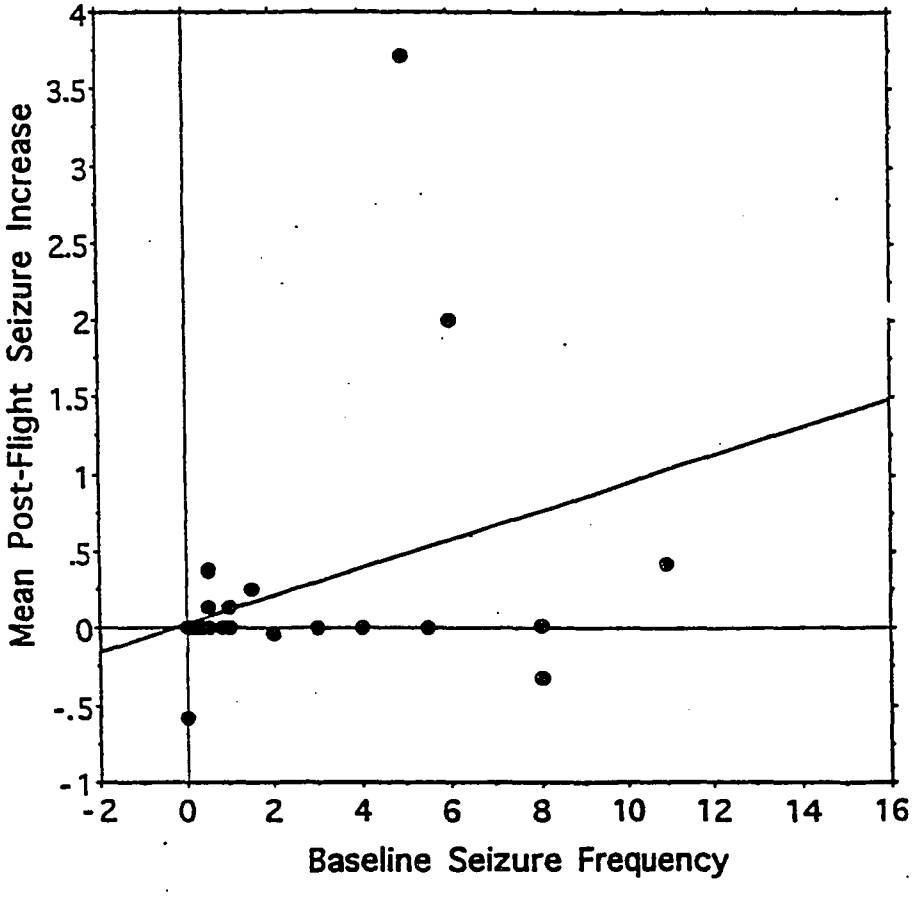

Figure 6: Baseline Seizure Frequency & Post-Flight Seizure Increase

Note. Outlier Baseline Seizure Frequency (55 seizures/month) not included

Chapter IV.

DISCUSSION

This study sought to empirically investigate clinical observations that air travel, particularly extended east-west flight, promotes seizures in individuals with epilepsy. Before interpreting the results of the study it should be noted that it was an exploratory and unprecedented investigation. The study's hypotheses were generated from patient report, clinical lore, and a synthesis of findings from diverse literature (such as on sleep, sleep and epilepsy, biological rhythms, and human factors in aerospace environments). It was also necessary to develop many of the methods used to investigate the relationships in question. Two of the most significant limitations of the study to consider before interpreting the results are 1) the issue of generalizability and 2) limitations due to the reliance on self-report data.

Study Limitations

Generalizability of the Sample

Although recruitment efforts were believed to have reached a broad spectrum of the epilepsy population, the resulting subject sample was small and deviates from the general epilepsy population by being almost entirely Caucasian, college educated, and mostly female. Most subjects also reported having very good control over their seizures.

The subject sample was almost entirely Caucasian and college educated which may reflect demographics of the general population that travels more frequently by air. That the subject sample was mostly female may reflect the participation of many staff members of the Epilepsy Foundation of America, a non-profit organization that is predominantly staffed by women. How representative this subject profile is to the population of individuals with epilepsy who fly is not known. There is an obvious need for additional studies with larger sample sizes to address this question.

Reliance on Self-Report Data

Although the self-monitoring of seizures is often requested by neurologists and found reliable by researchers (e.g., Groh, Tatzer, & Schubert, 1987), there were no independent or convergent measures to verify the veracity of subjects report of seizure frequency in this study. Increased confidence in this study's findings would be gained by replications using psychophysiological assessment and the report of household members.

Daily sleep monitoring can be effectively used to measure total sleep time as well as subjective assessments of sleep quality (for example, Bootzin & Nicassio, 1978). However, in this study there were no independent or convergent measures to verify the veracity of the subjects report about their sleep. For example, there is no means of determining if a subject retrospectively completed the self-monitoring schedule towards the end of the 15 day period after having failed to monitor their sleep on a day by day basis. As with the monitoring of seizures, the use of psychophysiological assessment and report of bed partners would increase the confidence regarding this data.

In addition to completing self-monitoring schedules for seizures and sleep in the EATQ, subjects were asked to complete a number of demographic questions, questions regarding their health habits, epilepsy history and medication use, and report information about their previous experiences with flying and their current air travel. For the most part, the veracity of subject's report for these sections of the EATQ cannot be verified. One exception was the ability to independently verify the approximate departure time, arrival time and length of flight reported by subjects through cross-checking with air passenger schedules (published by airline companies).

Evaluation of the Hypotheses

Air Travel and Post-Flight Seizures

Clearly, most subjects had no increase in seizures after flying. Many subjects flew without difficulty across considerable distances, across multiple time zones, and at all hours of the clock. However, this impunity to seizure increase was not enjoyed by all

subjects. For those subjects who experienced seizures during the 15 days of self-monitoring, seizures were three times more common after flying than before air travel (see Figure 2). This departure from random seizure occurrence suggests that for a subgroup of individuals with epilepsy (identified below) air travel is indeed a risk factor. The hypothesis that seizure will occur non-randomly by occurring more frequently after air travel than before air travel is therefore accepted.

Sleep Loss and Post-Flight Seizures

Sleep loss occurred for the day prior to air travel and for the day of air travel. There was also a significant rebound in sleep after this loss. The correlation between sleep loss and post-flight seizure increase (and post-flight seizure increase after transformation) was negligible (see Table 4). The hypothesis that sleep loss is associated with an increase in post-flight seizures was rejected.

The lack of relationship between sleep loss and seizure increase is surprising given the well established relationship between sleep loss and seizure promotion. It is also surprising, given that 76% of subjects reported that they recognize sleep loss as a trigger for their own seizures. One possible explanation to the lack of a relationship may be that the amount of sleep loss (and relatively lower levels of sleep "rebound") were not significant enough to have produced seizures. Some of the variability in sleep may have been lost to approximate and retrospective recording by subjects. The use of anticonvulsant medications may have also masked any relationship. It should also be noted that records of total sleep time were not sensitive to the quality of sleep, or even daytime sleepiness, which may have influenced seizure production.

Sleep Disruption and Post-Flight Seizures

The study inferred that sleep variability reflected departure from regular sleep patterns. Irregular sleep would predispose an individual with epilepsy to more frequent transitions in vigilance and more transitions from awake to sleep states (and visa-versa) and consequently may promote the occurrence of seizures. Sleep became more variable for the

day prior to and the day of air travel, as reflected by the standard deviation of TST (see Table 9). However, significant differences in the standard deviation of TST occurred more often for subjects without seizure increase than for subjects with post-flight seizure increase. The hypothesis that sleep disruption is associated with an increase in post-flight seizures was rejected.

Circadian Rhythm Disruption and Post-Flight Seizures

Circadian rhythm disruption as reflected in measures of distance traveled was associated with an increase in seizures after flying. The mean distance traveled was significantly greater for those with post-flight seizure increase, compared with those without an increase in seizures after flying. The hypothesis that a measure of circadian rhythm disruption is associated with an increase in post-flight seizures was accepted.

Baseline Seizure Frequency and Post-Flight Seizures

A significant relationship appears to exist between baseline seizure frequency and post-flight seizure increase—the less control an individual has over their seizures the greater the likelihood that traveling by air will promote an increase in seizure frequency. No specific baseline seizure frequency emerges that signifies when an individual is likely to experience an increase in post-flight seizures (in part due to the skewed distribution of baseline seizure frequency). However, the mean baseline rate of seizures for those who experienced post-flight seizure increase was 3.25 seizures per month (as opposed to 1.33 seizures for those without post-flight seizure increase). The hypothesis that baseline seizure frequency is associated with an increase in post-flight seizures was accepted.

Theoretical Implications of the Study

This study provides the first empirical data regarding the impact of air travel (a specific environmental circumstance/behavior) on seizures (brain dysfunction). Typically brain function (and dysfunction) is studied (and treated) as if environmental context, behavior, and cognition were irrelevant. Such a division between mind and body is reflected in the current management of epilepsy. The neurologist, defining epilepsy as a

pathological brain state, generally modifies brain dysfunction with anticonvulsants (i.e., treats the "body"); the psychologist manages the states of "mind" that result from epilepsy, such as low-self esteem, depression, personality problems or manages problem behavior such as poor medication compliance.

Studies of reflex epilepsies (for example, Forster, 1969), the observations of the relationships between sleep, vigilance, and seizures, and the use of classical and operant paradigms (behavioral and biofeedback) for seizure reduction have all contributed to a reductionist perspective on seizure genesis. Seizures can no longer be thought of as the random discharges of a damaged brain. Rather, seizures are part of a multivariate, multicausal process that includes physiological brain states (possible lesion or abnormality), circadian and ultradian rhythms, environmental stimuli, cognition (vigilance), learning, emotional responses and behavior. Such physiological, behavioral and mentalistic/cognitive variables have been integrated into complex biopsychosocial models of epilepsy (for example, Feldman & Paul, 1976; Fenwick, 1991).

The current study contributes to models of seizure genesis that include environmental and behavioral variables. Seizures appear to be promoted by extended air travel particularly for individuals whose epilepsy is less well controlled. Although the specific aspects or mechanism by which air travel contributes to seizures is not known, the study nevertheless empirically identifies a population and risk factors that had not previously been documented.

Of perhaps broader conceptual significance is the notion of "vulnerability" to brain dysfunction. Given that high baseline seizure frequency predicts post-flight seizure increase, it is intuitively reasonable that those with the least control over their seizures will be those most affected by challenges to the central nervous system—be they from medication changes, physical or psychological stress. "Vulnerability" that results in an exacerbation of symptoms may vary similarly in patients with other central nervous sytem disorders. Specifically, patients with the least control over their disorder may be most likely

to have an exacerbation of symptoms when challenged by some environmental and/or psychosocial stressor.

Clinical Implications of the Study

The results of the current study suggest that strategies may be effective in reducing the likelihood of an increase in seizures after flying. For example, circadian rhythm disruption, as reflected by distance traveled appears to be related to an increase in post-flight seizures. By articulating one long flight into two or more shorter flights with layovers, the risk of an increase in post-flight seizures may be reduced, particularly for those with high pre-flight seizure frequency.

Baseline seizure frequency may be a robust predictor of post-flight seizure increase. However, the utility of such a finding is unclear. It is interesting to note that the one subject in the current study who had a relatively high baseline seizure rate (eight seizures a month) and who had an actual decrease in post-flight seizures, chose to increase her medications for the week of her travels—apparently with some success in seizure control. There may be considerable clinical utility in predicting post-"challenge" seizure increase from baseline seizure rates. Should a neurologist treating a patient with poorly controlled seizures increase that patient's anticonvulsant medication during a trip requiring extended air travel? Such measures have been taken, both by patient's own initiative and by physician request (C. Lao Velez, personal communication, October, 1991) however, no study has been done on the efficacy of such an approach.

Future Research Questions

Many more questions remain than are answered by this initial investigation of the relationship between air travel and epilepsy. The five exploratory hypotheses pursued in this study were a select few of many interesting questions.

Variables that may impact seizures but were not evaluated in the dissertation include (but are not limited to) medication usage, flight altitude, and psychological attributes, such as trait anxiety. Maintaining therapeutic blood levels of anticonvulsant medications is of

obvious importance for most epileptics. However, maintaining an appropriate blood level may be more difficult when traveling across time-zones. The question arises as to whether the epileptic traveler should continue their regimen on the time schedule of their place of departure or adjust to taking medications according to local time. Flight altitude may effect seizure threshold as a consequence of differences in air pressure. Ames (1982) notes that seizures are promoted by changes in blood pH due to hyperventilation. Psychological traits and states, such as anxiety, were not investigated in this study but may contribute to the understanding of why some individuals with epilepsy appear more prone to seizures during and/or after flying. As previously mentioned hyperventilation, that results from anxiety states, has been implicated in the generation of seizures (Ames, 1982).

The notion of "vulnerability" previously mentioned may be worthy of future investigation. It may be interesting to investigate whether base-rates of symptom production of other central nervous system disorders are predictive of the frequency of such symptoms after a "challenge" be it from a physical or psychosocial stressor.

In addition to new questions that arise from this study new methods are suggested. It was expected that air travel would promote seizures through sleep loss and sleep disruption. This model was not supported in the current study perhaps as a consequence of insensitive and/or inaccurate sleep measures. Different approaches for assessing sleep may result in greater sensitivity to a relationship between sleep loss and sleep disruption and an increase in post-flight seizures. For example, the recruitment of bed partners may have promoted more accurate sleep records. The use of psychophysiological devices, such as a wrist actigraph may be appropriately used to this end. The possibility of using ambulatory EEG before, during, and after flight may provide interesting information regarding sleep as well as ictal behavior during these phases.

Future investigations into the relationship of air travel to seizures may want to consider other aspects of seizures and sleep. Measures of sleep and seizure quality were not employed in this research. It is possible that air travel results in a decrement of the

quality of sleep that is not accounted for by recording sleep time. Similarly, seizures vary in intensity and duration within subjects. It is possible that air travel promotes seizures to be of greater intensity and duration as well as greater frequency.

APPENDIX A

Epilepsy and Air Travel Questionnaire

Thank you for participating in the Epilepsy and Air Travel study!
The purpose of this questionnaire is to learn more about how people with epilepsy experience air travel. This information may help health care providers help those with epilepsy who experience difficulties with air travel.

Your participation is entirely voluntary: you are not asked to write your name and your responses will be kept strictly confidential.

There are 4 parts to this questionnaire:
Part 1--asks you questions about yourself, your lifestyle, and your epilepsy
Part 2--asks you to record your seizures and sleep for the week before your flight
Part 3--asks you about your flight(s)
Part 4--asks you to record your seizures and sleep for the week after your flight

Please note that you start filling out the questionnaire on the 7th day before your flight, and you record your seizures and sleep each day, for the week before and the week after your flight.
This questionnaire only concerns your experiences before and after flying to your destination (in one direction).

Once the questionnaire is complete please return it in the envelope provided.

If you have any questions or comments about this study please contact
Tracy Trevorrow, M.S.
Epilepsy and Air Travel Study
2430 Campus Road
Honolulu, Hawaii 96822 Phone (808) 957-3032

Your participation is greatly appreciated and we would like to share with you the results of the study. If you would like to be sent a copy of the results please write your address below.

_____
_____
_____

Part 1: About You, Your Lifestyle, and Your Epilepsy
Complete this part anytime prior to your flight.

Today's date
(day/month/year) ___/___/___

1. Sex: ___ Male ___ Female
2. Age: ___
3. Ethnicity/Race: _____
4. Education: Last grade of high-school completed ___
   Years of post high-school education ___
5. Marital Status: ___ Never Married ___ Married/living together
   ___ Separated/Divorced/Widowed
6. Occupation: _____
7. Do you work rotating shifts or overnight shifts? ___ Yes ___ No
8. What types of seizures have you had?
   ___ Don't know ___ Simple and/or Complex Partial
   ___ Generalized/Grand Mal ___ Petit Mal/Absence
   ___ Pre-seizure auras ___ Other _____
9. Which kind of seizures do you have most often? _____
10. What was the initial cause of your epilepsy?_____
11. How old were you when you had your first seizure? ____
12. When do you currently experience seizures?
    ___ waking up ___ during the day & evening ___ while sleeping
13. How aware are you of having a seizure?
    ___ I am aware of each seizure
    ___ I am aware of most seizures
    ___ I am aware of few of my seizures
    ___ I cannot tell when I have had a seizure

14. On average how many seizures per month have you had in the last year? ____

15. What medications (if any) are you currently taking for your epilepsy?

Medication	Amount	Time(s) taken
_____	_____	_____
_____	_____	_____
_____	_____	_____

16. What other medications are you currently taking?

Medication	Amount	Time(s) taken
_____	_____	_____
_____	_____	_____

17. On the average night, how many hours do you sleep? ____
18. What time do you usually go to bed on weekday (Mon-Fri)? ____
19. What time do you usually wake up on weekdays (Mon-Fri)? ____
20. How many naps do you take on an average day? ___average week? ___
21. How long is your average nap? ____ hours ____ minutes

22. How much of the following do you consume?

Beer (cans/bottles) per day ____	Wine/Wine coolers per day ____
Mixed drinks (glasses) per day ____	Alcoholic drinks per week ____
How many cigarettes per day ____	Coffee (cups) per day ____

23. How many flights have you taken in the last month? ____
24. How many flights have you taken in the last year? ____
25. How many flights have you taken since you first started having seizures?
    (If more than 100 please approximate to the nearest 50) _____
26. Have you ever avoided or seriously considered not taking a flight because of a fear of flying? ___ Yes ___ No
27. If "Yes" what were you fearful of? _____
28. Have you worried about having a seizure while flying? __Yes __No
29. How many times have you had a seizure (or seizures) during the week *before* a flight? ___
30. How many times have you had a seizure while on a plane? ___
31. How many times have you had a seizure (or seizures) during the week *after* air travel? ___
32. Indicate if the following appear to "set off" or "trigger" your seizures
    __ skipping meals __ being short on sleep
    __ too much sleep __ emotional stress
    __ physical stress __ menstrual cycle
    __ flashing lights __ coffee/tea
    __ alcohol __ pain
    __ change in medication. Describe _____
    __ other _____

Part 2: The Week *Before* Your Flight

Fill this out each day, starting on the 7th day before your flight.

Step 1. Fill the top row with the dates of the 7 days before your flight.
Step 2. Write the number of seizures you had in each of the hour periods (leave blank if you had no seizures during that hour).
Step 3. Each day, after you wake-up, show when you slept with a straight line.

Date➔							Flight Day
6 am							
7 am							
8 am							
9 am							
10 am							
11 am							
Noon							
1 pm							
2 pm							
3 pm							
4 pm							
5 pm							
6 pm							
7 pm							
8 pm							
9 pm							
10 pm							
11 pm							
Midnight							
1 am							
2 am							
3 am							
4 am							
5 am							

Part 3: About Your Flight(s)

Fill this out as soon as possible after your flight(s)

1. Name and location of your airport of departure
   _____
2. Name and location of airports of connecting flight(s)
   _____
   _____
3. Name and location of your airport of final destination
   _____
4. What airline(s) did you travel on? _____
5. What time did you first take-off?
   (time at place of departure) _____ am/pm (circle)
6. What was the local time when you landed?
   e.g., if you flew from L.A. to N.Y., what was the N.Y. time?
   _____ am/pm (circle)
7. How many hours & minutes were you actually "in flight"?
   ____ hours ____ minutes
8. Describe any changes in your scheduled take-off and arrival times.
   _____
9. How much did you sleep on the plane? ____ hours ____ minutes
10. How many of the following did you consume during your travel?
    (include consumption at airports)

Beer (cans/bottles)	____	Wine/Wine coolers	____
Mixed drinks (glasses)	____	Coffee (cups)	____
Non-alcoholic beverages (glasses)	____	Cigarettes	____
Major Meals (b-fast,lunch,dinner)	____	Snacks (e.g.,fruit)	_____

11. What medications (if any) did you take for your epilepsy during your trip-from the day you left?

Medication	Amount	Time(s) taken
_____	_____	_____
_____	_____	_____

12. Describe any changes to your regular medication use during the week prior to and the week after your flight.
    _____
    _____
13. Your trip was mostly for...
    ____ Business/Work ____ Pleasure/Vacation ____ Both
    ____ Other (explain)_____

Part 4: The Week *After* Your Flight

Fill this out each day, for the 7 days after your flight(s).

Step 1. Fill the top row with the dates of the 7 days after your flight.
Step 2. Write the number of seizures you had in each of the hour periods
Step 3. Each day after you wake-up show when slept with a straight line

First day after your flight
(or may be day of arrival)

Date	↓						
6 am							
7 am							
8 am							
9 am							
10 am							
11 am							
Noon							
1 pm							
2 pm							
3 pm							
4 pm							
5 pm							
6 pm							
7 pm							
8 pm							
9 pm							
10 pm							
11 pm							
Midnight							
1 am							
2 am							
3 am							
4 am							
5 am							

APPENDIX B

A Letter of Introduction: the Epilepsy and Air Travel Study

Your neurologist Dr. _____ would like you to consider participating in a study of the effects of air travel on epilepsy.

Flying can be a stressful experience for anyone but it may be especially stressful for someone with epilepsy. Some individuals with epilepsy fear of having a seizure during the flight. Others worry about the possibility of having a seizure in a foreign place where medical help is not available or unfamiliar. Still other people with epilepsy have trouble taking their medications on the right schedule when they fly across many time zones.

The Epilepsy and Air Travel Study, is a study funded by the Epilepsy Foundation of America, to investigate people's experience with having epilepsy and traveling by air. This study intends to provide health care professionals, such as your neurologist, with a clearer picture of problems for people with epilepsy who fly. This study may lead to the development of ways to reduce the stress and strain of flying for those with epilepsy.

To participate you must have epilepsy and be planning on traveling by air in the next six months. Participation involves completing a questionnaire about yourself, your epilepsy, and your previous experiences with flying. Participation also involves keeping a log of your seizures and your sleep before and after your next flight. You are not asked to include your name on the questionnaire and all the information will be kept strictly confidential.

If you are interested in participating please tell your neurologist or the neurology office staff and they will be happy to give you the questionnaire. Thank you for considering to participate in this study. If you would like to find out more about the study please contact...

The Epilepsy & Air Travel Study
c/o Tracy Trevorrow
2430 Campus Road University of Hawaii-Manoa,
Honolulu, Hawaii 96822
Phone (808) 956-6432 or call
The Epilepsy Foundation of Hawaii @ (808) 523-7705

APPENDIX C

Fragebogen über Epilepsie im Zusammenhang mit Flugreisen

Für die Teilnahme an der Studie über Epilepsie und Flugreisen danken wir Ihnen recht herzlich. Ziel dieses Fragebogens ist es, näheres darüber zu erfahren, wie Personen mit Epilepsie Flugreisen erleben. Mit Hilfe dieser Informationen wird es zukünftig möglich sein, eventuell auftretende Probleme bei Flugreisen besser zu bewältigen.

Ihre Teilnahme ist absolut freiwillig: Sie brauchen Ihren Namen nicht anzugeben und Ihre Antworten werden streng vertraulich behandelt.

Dieser Fragebogen ist in 4 Teile aufgeteilt:

Teil 1 enthält allgemeine Fragen über Sie selbst, Ihre Lebensweise, und über Ihre Epilepsie

Teil 2 tragen Sie hier bitte Anfallshäufigkeit und Schlafdauer in der Woche vor Ihrem Flug ein

Teil 3 Fragen über Ihren Flug/Flüge

Teil 4 hier werden wie in Teil 2 Anfallshäufigkeit und Schlafdauer in der Woche nach Ihrem Flug/Flügen eingetragen

Bitte schicken Sie uns den Fragebogen in dem frankierten Briefumschlag, den Sie erhalten haben, zu.

Wir danken Ihnen sehr für die Teilnahme an dieser Studie. Wir hoffen, daß Ihre Mitarbeit dazu beitragen wird, Menschen mit Epilepsie zukünftig besser zu helfen.

Teil 1: Fragen über Sie, Ihre Lebensweise und Epilepsie

Bitte füllen Sie diesen Teil irgendwann vor Ihrem Flug aus.

Datum
(Tag/Monat/Jahr) __/__/__

1. Geschlecht: ___ männlich ___ weiblich
2. Alter: ___
3. Nationalität _____
4. Schulbildung: _____
5. Familienstand: ___ ledig ___ verheiratet __ getrennt lebend
   ___ geschieden ___ verwitwet ___ andere _____
6. Beruf: _____
7. Arbeiten Sie im Schichtdienst oder Nachtschichten __ Ja __Nein
8. Welche Art/en von Anfällen haben Sie?
   - ____ weiß nicht
   - ____ Partiell, Fokal odor Komplex
   - ____ Generalisiert/Grand Mal
   - ____ Psychomotorische Anfall
   - ____ Petit Mal
   - ____ Absence
   - ____ Aura vor dem Anfall
   - ____ andere

   _____
9. Wann haben Sie Anfälle
   - ____ tagsüber/abends
   - ____ im Schlaf
   - ____ beim Einschlafen
   - ____ beim Erwachen
10. Wie bewußt nehmen Sie Anfälle wahr?
    - ____ich bin nehme jeden Anfall bewußt wahr
    - ____ich nehme die meisten, aber nicht alle Anfälle bewußt wahr
    - ____ ich nehme nur wenige Anfälle wahr
11. Alter beim ersten Anfall ____
12. Ungefähre Anzahl von Anfällen pro Monat im letzten Jahr ___
13. Welche Medikamente (falls überhaupt) nehmen Sie zur Zeit wegen Ihrer Epilepsie ein?

Medikament	Menge	wann
_____	_____	_____

14. Welche Medikamente nehmen Sie sonst noch?

Medikament	Menge	wann
_____	_____	_____

15. Wie viele Stunden schlafen Sie normalerweise?..... ____
16. Um wieviel Uhr gehen Sie normalerweise
    werktags schlafen (Mo-Fr)?..... ____
17. Um wieviel Uhr wachen Sie normalerweise
    werktags auf (Mo-Fr)?..... ____
18. Falls Sie tagsüber Nickercheu machen geben Sie an, wieviele und
    wie lange jeweils? Anzahl _____Dauer (des Nickerchens) ____
19. Wieviel konsumieren Sie normalerweise innerhalb von 24 Stunden
    Bier (Flaschen)..... ___
    Wein (Gläser)..... ___
    Drinks (Gläser).... ___
    Kaffee (Tassen)..... ___
    Zigaretten..... ___
20. Wie oft nehmen Sie Schlaftabletten ein in einem Monat?..... ____
21. Wie oft in der Woche trinken Sie alkoholische Getränke..... ____
22. Anzahl der Flüge im letzten Monat ..... ____
23. Anzahl der Flüge im letzten Jahr ..... ____
24. Wie oft sind Sie schon geflogen, seitdem Sie zum ersten
    Mal Anfälle hatten?..... ____
25. Haben Sie schon einmal auf einen Flug verzichtet, oder sich
    dies ernsthaft überlegt, aus Angst vor dem Fliegen __ Nein ___Ja
26. Wenn "ja" - wovor hatten Sie Angst? _____
27. Hatten Sie Angst, während des Fluges einen Anfall
    zu bekommen?.....___ Nein ___ Ja
28. Wie oft hatten Sie in der Vergangenheit einen Anfall (oder Anfälle)
    während des
    Fluges oder in der Woche nach dem Flug?..... ____
29. Geben Sie an, ob folgendes bei Ihnen ein Anfall ausgelösen kann:
    ____ keine Mahlzeit
    ____ Schlafmangel
    ____ zu veil Schlaf
    ____ psychischer Stress
    ____ körperliche Belastung
    ____ Wechsel von Medikamenten--nähere Angaben
    ____ Kaffee, Tea
    ____ Alkohol
    ____ Menstruation
    ____ Schmerzen--Art der Schmerze
    ____ andere
    _____

Teil 2: Die Woche vor Ihrem Flug

Beginnen Sie bitte 7 Tage vor Ihrem Flug damit, diesen Abschnittauszufüllen

Schritt 1. Tragen Sie in die oberste Reihe das jeweilige Datum ein, beginnend mit dem 7. Tag vor Ihrem Flug.

Schritt 2. Schreiben Sie die Anzahl von Anfällen auf, die Sie in jeder Stunde hatten (wenn Sie keinen hatten, lassen Sie das Kästchen frei).

Schritt 3. Geben Sie in der untersten Reihe die ungefähre Anzahl der Stunden an, die Sie in dem 24-Stunden-Zeitraum geschlafen haben.

Datum→								Tag des Fluges
6 :00								
7:00								
8:00								
9:00								
10:00								
11:00								
12:00								
13:00								
14:00								
15:00								
16:00								
17:00								
18:00								
19:00								
20:00								
21:00								
22:00								
23:00								
24:00								
1:00								
2:00								
3:00								
4:00								
5:00								

Teil 3: Über Ihren Flug / Ihre Flüge

Füllen Sie bitte diesen Teil so bald wie möglich nach Ihrem Flug/Flügen aus.

1. Name/Ort des Abflug-Flughafens

   _____

2. Name/Ort des Flughafens, wo Sie umsteigen

   _____

3. Name/Ort des Ankunftsflughafens

   _____

4. Um wieviel Uhr sind Sie abgeflogen (Ortszeit des Abflugs)...

   _____

5. Um wieviel Uhr sind Sie angekommen (Ortszeit)..... _____
6. Wie viele Stunden sind Sie geflogen?..... _____
7. Wie lange haben Sie im Flugzeug geschlafen?

   ____Stunden ____Minuten

8. Wenn Sie einen Aufenthalt zwischen den Flügen hatten, wieviele Stunden haben Sie geschlafen?.....____Stunden ____Minuten
9. Wieviel haben Sie während Ihrer Reise getrunken bzw. gegessen? (einschließlich des Aufenthalt auf dem Flughafen)

   Bier (Flaschen)..... ____
   Wein (Gläser)..... ____
   Kaffee (Tassen)..... ____
   Nicht-alkoholische Getränke..... ____
   Zigaretten..... ____
   Hauptmahlzeiten (Frühstück, Mittag-, Abendessen)... ____
   Snacks (z.B. Obst, Kekse, Süßigkeiten, Kuchen)..... ____

10. Welche Medikamente (falls überhaupt) haben Sie während Ihrer Reise wegen der Epilepsie eingenommen?

Medikament	Menge	wann
_____	_____	_____
_____	_____	_____
_____	_____	_____

11. Haben Sie andere Medikamente als sonst eingenommen?

    _____

12. Beschreiben Sie den Unterschied zu Ihrer sonstigen Medikamenteneinnahme in der Woche vor und in der Woche nach Ihrem Flug._____

Teil 4: Die Woche nach dem Flug

Füllen Sie diesen Abschnitt am Tag Ihres Fluges und jeden Tag bis zum 7. Tag danach aus.

Schritt 1. Tragen Sie in die oberste Reihe das jeweilige Datum ein, beginnend mit dem 7. Tag vor Ihrem Flug.
Schritt 2. Schreiben Sie die Anzahl von Anfällen auf, die Sie in jeder Stunde hatten (wenn Sie keinen hatten, lassen Sie das Kästchen frei)
Schritt 3. Geben Sie in der untersten Reihe die ungefähre Anzahl der Stunden an, die Sie in dem 24-Stunden-Zeitraum geschlafen haben

Datum>						
6 :00						
7:00						
8:00						
9:00						
10:00						
11:00						
12:00						
13:00						
14:00						
15:00						
16:00						
17:00						
18:00						
19:00						
20:00						
21:00						
22:00						
23:00						
24:00						
1:00						
2:00						
3:00						
4:00						
5:00						

APPENDIX D

Epilepsy and Air Travel Questionnaire Back Translation
(German to English)
By Ilse Maria Zalaman
April 1991

(Page 1)

Questionnaire about Epilepsy
in Connection with Air Travel

The objective of this questionnaire is to know more about how people, who are suffering from epilepsy, experience flying. By providing this information it will be possible to handle eventual occurrence of problems in a better way.

Your participation is absolutely voluntary: you don't have to write down your name and your answers will be treated strictly confidential.

This questionnaire is divided into 4 parts:

Part 1 contains general questions about yourself, your way of life, and about your epilepsy.

Part 2 please enter the number of attacks and the amount of sleep per week, one week before your actual flight.

Part 3 questions about your flight/flights

Part 4 is just like part 2. You have to write down the number of attacks and amount of sleep per week after your flight(s)

Please return the questionnaire in the provided stamped envelope.

We would like to thank you very much for participating in this study. We are hoping that your participation will contribute to helping people with epilepsy in the future.

(page 2)

Part 1: Questions about Yourself, Your Way of Life,
and Epilepsy
Please fill this part out before your flight.

Date
(day/month/year) __/__/__

1. Sex: __ male __ female
2. Age: __
3. Nationality: _____
4. Education: _____
5. Marital status: __ single __ married __ separated __ divorced, __ widowed, __ other
6. Occupation: _____
7. Do you do shift work or work the night shift? ___ Yes ___ No

8. What kinds of attacks do you have?
   ___ Don't know
   ___ Partial, focal or complex
   ___ Generalized/grand Mal
   ___ Petit Mal
   ___ Absences
   ___ Aura before the attack
   ___ Other _____
9. When do you have attacks
   ___ during the day/in the evening
   ___ while sleeping
   ___ when falling asleep
   ___ when waking up
10. How aware are you of the attacks?
   ___ I am aware of each attack
   ___ I am aware of most, but not all
   ___ I am only aware of a few
11. Age at the first attack ___
12. Attacks per month during the last year (on the average) ___
13. What kind of medication, if any, do you take for your epilepsy?

Medication	Amount	When
_____	_____	_____
_____	_____	_____
_____	_____	_____

14. What other medications do you take?

Medication	Amount	When
_____	_____	_____
_____	_____	_____
_____	_____	_____

(page 3)

15. How many hours do you normally sleep? ____
16. At what time do you generally go to sleep during the week (Mon-Fri)? ___
17. At what time do you generally wake up in the morning (Mon-Fri)? ___
18. How many naps do you generally take during the day? ___

19. How much do you generally drink within 24 hours?
   beer (bottles)..... ___
   wine (glasses)..... ___
   mixed drinks (glasses)..... ___
   coffee (cups)..... ___
   How many cigarettes do you smoke? ___
   How many sleeping pills do you take? ___
20. How often do you drink (alcohol) during the week? ___
21. How many times have you traveled by plane since your first attack? ___
22. Number of flights taken within the last month ___
23. Number of flights for the past year ___
24. have you ever canceled a flight or were you seriously thinking of canceling because you were afraid of flying? ___ No
25. If "Yes" what were you afraid of? _____
26. Were you afraid of having an attack during the flight? ___ No ___ Yes

27. How many attacks did you have during the flight or during the week after the flight?
28. Indicate whether the following can trigger an attack for you:
    ___ not eating
    ___ lack of sleep
    ___ too much sleep
    ___ psychological stress
    ___ somatic stress
    ___ changing to another medication (specify) _____
    ___ coffee, tea
    ___ alcohol
    ___ menstruation
    ___ pain, which kind _____
    ___ other_____

(page 4)

Part 2: The Week before Your Flight
Would you please fill in this section one week before your flight

Step 1: In the first row would you please enter the date for each day before your flight.
Step 2: Please record the number of attacks per hour
    (if you did not have any please leave the box empty).
Step 3: Please indicate the hours that you slept by drawing a straight vertical line.
Step 4: In the last row would you please indicate the approximate amount of sleep that you got within a 24 hour period.

(page 5)

Part 3: About Your Flight(s)
Would you please fill out this part immediately following your flight(s) or as soon after as possible thereafter.

1. Name and location of airport from which you are departing
    _____
2. Name and location of the airport, where you have to change planes
    _____
3. Name and location of the airport where you did arrive
    _____
4. At what time did your plane take off (local time) _____
5. At what time did you arrive (local time) _____
6. How many hours were you in the air? _____
7. How many hours did you sleep on the plane?___Hours ___Minutes
8. If you had time between flights, how many hours did you sleep?
    ___ Hours ___Minutes
9. While traveling how much did you have to eat and drink
    (including your stay at the airport)
    beer (bottles)..... ___
    wine (glasses)..... ___
    coffee (cups)..... ___
    nonalcoholic beverages..... ___
    cigarettes..... ___
    main meals (breakfast, lunch, dinner) ___
    snacks (e.g. fruit, cookies, sweets, cakes) ___

10. Which kind (if any) anti-epileptic drugs did you take while traveling?
Medication _____Amount_____When_____
11. Did you take (ingest) any other drugs?
12. The purpose of this trip was mainly ___ vacation
___ official
___ other reason

(page 6)

Part 4: The Week after Your Flight
Would you please fill out this section 7 days after your flight

Step 1: In the first row would you please enter the date for each day before your flight.
Step 2: Please record the number of attacks per hour
(if you did not have any please leave the box empty).
Step 3: Please indicate the hours that you slept by drawing a straight vertical line.
Step 4: In the last row would you please indicate the approximate amount of sleep that you got within a 24 hour period.

APPENDIX E

Guide to Data Abbreviations and Data Set

Data Abbreviation		Variable Description
ID		Identification of recruitment source
	HI-N	Hawaiian neurologist
	VA-C	Epilepsy Foundation of America conference in Virginia
	EF-A	Epilepsy Foundation of America Affiliate
	Individual	Individual responding to mass media announcement
	Germany	Germany epilepsy center patient
Sex		
	Male	
	Female	
Age		
Ethnicity/Race		
	Asian	Asian racial and cultural origin or background
	White	Caucasian
Education		In years, e.g. 12 = highest level of education was high school
M. Stat		Marital Status
	Sing	Single
	S.D.W.	Separated, Divorced, Widowed
	Mard	Married
Shift		Shiftwork, does the participant work different work shifts?
Part		Partial Seizures, the participant has partial seizures
Gen		General Seizures, the participant has general seizures
Pet/Abs		Petit Mal or Absence Seizures, the participant has these seizures
Aura		Aura, the participant experiences an aura prior to seizures
Age 1 fit		Age participant experienced their first seizure (in years)

Fit/Mth	Number of seizures per month for past year before study
#Meds	Number of antiseizure medications the participant is taking
HrSlp	Hours of sleep per weeknight participant typically has
Naps	Does the participant typically nap?
Beer	Consumption of beer (per can/bottle) in average day
Wine	Consumption of wine (per glass) in average day
MixDrk	Consumption of mixed drink (per glass) in average day
Coff	Consumption of coffee (per cup) in average day
X-etoh	Consumption of alcoholic drinks (per serving) in average week
FlyLsMth	Number of flights taken last month (prior to participation)
FlyLstYr	Number of flights taken last year (prior to participation)
FlyPstFit	Number of flights taken since having epilepsy
AvoFly	Does the participant avoid flying?
WorFlyFit	Does the participant worry about having a seizure while flying?
#fitPstFly	Number of previous flights remember having an increase in seizures
SkpFud	Does skipping a meal trigger a seizure?
LowSlp	Does being low in sleep trigger a seizure?
HghSlp	Does getting too much sleep trigger a seizure?
PsySts	Does psychological stress trigger a seizure?
PhySts	Does physical exertion trigger a seizure?
ChgMed	Does a change in medication trigger a seizure?
CofTea	Does coffee or tea trigger a seizure?
etoh	Does use of alcohol trigger a seizure?
Period	Does onset of menstrual cycle trigger a seizure?
Pain	Does pain trigger a seizure?
Flight	Name of the places of departure and arrival
TrvTim	Travel Time, time in the air (in minutes)

TZ	Times Zones crossed
TThr/2	Time in hours divided by two (used in ICAO formula)
TZup4	Number of time zones crossed above four (used in ICAO formula)
DepCo	Time of departure coefficient (used in ICAO formula)
ArrCo	Time of arrival coefficient (used in ICAO formula)
ICAO	ICAO formula for flight crew recovery time (in tenths of a day)
Direct	Flight direction
SlpFly	Sleep experienced during flight (in minutes)
BerFly	Beer consumed while in transit (in bottles/cans)
WinFly	Wine consumed while in transit (in glasses)
MixFly	Mixed drink consumed while in transit (in glasses)
CofFly	Cups of coffee consumed while in transit
CigFly	Number of cigarettes consumed while in transit
BigFud	Number of major meals consumed while in transit
Snack	Number of snacks consumed while in transit
NonAlc	Number of non-alcoholic drinks while in transit
Slp-7 to Slp+7	Hours of sleep per 24 hour period from day 1 to day 15
AvPreSlp	Mean hours of sleep for the 7 days prior to flying
AvPstSlp	Mean hours of sleep for the flight day and 7 days post-flight
Fit-7 to Fit+7	Number of seizures per 24 hours period from day 1 to day 15
mean pre fit	Mean number of seizures for 7 days before flying
mean post fit	Mean number of seizures for flight day and 7 days after flying
sum sz pre	Sum of seizures for 7 days before flying
sum sz post	Sum of seizures for flight day and 7 days after flying
sz mean diff	Difference between mean seizures pre and post flight
sum sz diff	Difference between sum of seizures pre and post flight
1/x Fit/mth + 1	Seizure per month plus 1 and then inverted (transformed variable)

distance	Distance of flight (in miles)
1/x mean sz diff+ 1	Mean seizure difference plus 1 then inverted (transformed variable)

	ID	Sex	Age	Ethnic	Educ.	M.Stat	Shift?	Part	Gen	Pet/Abs	Aura
1	HI-N	Female	33	Asian	15	Sing	No	No	yes	no	no
2	HI-N	Female	42	Asian	14	Sing	No	No	yes	no	yes
3	VA-C	Male	49	White	22	S.D.W.	No	No	yes	no	yes
4	VA-C	Male	60	•	16	Mard	No	No	no	yes	no
5	EF-A	Male	47	White	19	Mard	No	No	yes	no	no
6	Indiv	Male	48	White	18	Mard	No	No	yes	yes	yes
7	EF-A	Male	54	White	21	Mard	No	No	yes	no	no
8	EF-A	Female	30	White	12	Mard	No	Yes	no	no	no
9	Indiv	Female	37	White	16	Sing	No	No	yes	no	yes
10	Indiv	Female	48	White	19	Sing	No	Yes	yes	no	no
11	Hosp	Female	23	•	12	Sing	No	No	no	yes	no
12	Indiv	Female	43	White	16	S.D.W.	No	No	yes	no	no
13	Indiv	Female	27	White	14	S.D.W.	Yes	No	yes	yes	no
14	Indiv	Female	46	White	22	Mard	No	Yes	yes	no	yes
15	EF-A	Female	27	White	16	Mard	No	No	yes	no	yes
16	EF-A	Female	28	White	16	Mard	No	No	yes	no	no
17	EF-A	Female	33	White	13	Mard	No	No	no	yes	no
18	Indiv	Male	38	White	17	Sing	No	No	yes	no	yes
19	Indiv	Female	55	•	•	Mard	No	No	yes	yes	yes
20	Indiv	Female	18	Asian	13	Sing	No	Yes	yes	yes	yes
21	Germ	Male	33	White	13	Sing	No	Yes	no	yes	no
22	EF-A	Female	29	White	18	Mard	No	No	yes	no	no
23	HI-N	Female	26	Asian	19	Sing	No	No	yes	yes	yes
24	Germ	Female	38	White	12	Mard	No	No	no	yes	yes
25	Indiv	Female	24	White	16	Mard	No	No	yes	no	yes
26	Indiv	Female	28	White	16	Mard	No	Yes	yes	no	no
27	Indiv	Female	45	White	16	Mard	No	No	yes	yes	yes
28	EF-A	Female	46	White	17	Mard	Yes	Yes	no	no	no
29	Indiv	Female	29	White	22	Sing	Yes	Yes	yes	no	yes
30	Indiv	Female	70	White	17	Mard	No	Yes	yes	no	no
31	Indiv	Male	58	White	20	Mard	No	Yes	yes	no	yes
32	Indiv	Female	32	White	12	Sing	No	Yes	yes	no	no
33	EF-A	Female	43	White	14	Mard	No	Yes	yes	no	yes
34	Indiv	Male	9	White	3	Sing	No	Yes	yes	no	yes
35	EF-A	Male	41	White	16	Sing	•	Yes	yes	yes	yes
36	EF-A	Female	42	White	16	Mard	No	Yes	yes	no	no
37	EF-A	Male	31	White	12	Sing	Yes	Yes	no	no	no

	Age1fit	Fit/mth	#Meds	HrSlp	Naps	Beer	wine	mixDrk	Coff	Cigs	X-etoh
1	8.0	.30	2	7.00	no	0	0	0	2.00	0	0
2	3.0	6.00	2	7.00	no	0	1.00	1.00	4.00	0	.50
3	14.0	.50	1	6.00	no	0	0	0	1.00	15.00	0
4	38.0	.56	1	7.00	no	.50	0	.50	2.00	0	4.00
5	26.0	0	1	7.50	no	0	0	0	4.00	0	2.50
6	•	.12	0	7.00	no	0	0	0	2.50	0	0
7	15.0	0	1	6.00	no	0	0	0	0	0	0
8	.5	1.00	0	8.00	no	0	1.00	0	3.00	0	4.00
9	17.0	0	1	6.00	yes	0	0	0	0	0	0
10	44.0	8.00	1	7.00	no	0	0	0	1.50	0	0
11	7.5	0	1	7.00	no	0	0	0	3.00	0	0
12	38.0	.24	1	6.50	yes	0	0	0	7.00	30.00	0
13	19.0	0	1	5.50	no	0	0	0	0	0	0
14	20.0	.50	1	7.50	no	1.00	0	0	7.00	0	5.50
15	3.0	0	1	8.50	no	0	0	0	0	0	0
16	19.0	0	1	9.50	no	0	0	0	0	0	0
17	30.0	11.00	2	8.00	no	0	0	1.00	4.00	20.00	4.00
18	26.0	2.00	1	4.00	no	0	0	0	0	0	0
19	44.0	0	1	8.00	yes	0	0	0	4.00	0	0
20	12.0	5.00	1	7.00	no	0	0	0	2.00	0	0
21	4.0	4.00	2	6.50	no	0	0	0	5.00	30.00	0
22	25.0	.12	1	7.50	no	0	0	0	0	0	0
23	1.0	1.50	1	8.50	yes	0	0	0	0	0	0
24	5.0	5.50	2	6.75	yes	0	0	0	0	0	0
25	5.0	.08	2	10.00	yes	0	0	0	2.00	0	0
26	11.0	3.00	1	8.00	no	0	0	0	2.00	0	0
27	11.0	0	2	7.50	no	0	0	0	0	0	1.00
28	35.0	1.00	1	7.00	no	0	0	0	0	0	0
29	1.0	.80	1	7.00	no	0	0	0	8.00	0	0
30	57.0	0	1	6.00	yes	0	2.00	0	0	0	14.00
31	56.0	.50	2	9.00	yes	0	1.00	0	0	0	7.00
32	7.0	.33	2	7.50	no	0	0	0	2.00	0	0
33	30.0	8.00	2	7.50	no	0	0	3.00	7.00	0	3.00
34	.5	55.00	3	9.00	no	0	0	0	0	0	0
35	22.0	•	4	8.50	yes	1.00	.50	0	1.00	0	3.00
36	12.0	1.00	2	9.00	yes	0	0	0	3.00	0	0
37	6.0	1.00	2	6.25	yes	0	0	0	5.00	0	0

	FlyLstMth	FlyLstYr	FlyPstFit	AvoFly	WorFlyFit	#fitPstFly	SkpFud	LowSlp	HghSlp
1	0	0	6.00	no	no	0	no	yes	no
2	1.00	7.00	116.00	no	yes	67.00	no	yes	no
3	2.00	5.00	100.00	yes	yes	2.00	yes	yes	no
4	4.00	35.00	400.00	no	no	0	no	yes	no
5	2.00	19.00	1000.00	no	no	0	yes	yes	no
6	2.00	12.00	100.00	no	no	0	no	no	no
7	0	20.00	100.00	no	no	0	no	yes	no
8	0	12.00	100.00	no	yes	12.00	yes	no	no
9	0	6.00	35.00	no	no	0	no	yes	no
10	0	12.00	24.00	no	no	9.00	yes	yes	no
11	0	0	1.00	no	no	0	no	no	no
12	0	1.00	1.00	yes	yes	0	yes	yes	no
13	0	1.00	7.00	no	no	0	yes	yes	no
14	4.00	14.00	100.00	no	yes	1.00	no	yes	no
15	0	6.00	30.00	no	no	0	no	yes	no
16	2.00	10.00	34.00	no	no	2.00	no	yes	no
17	4.00	18.00	50.00	yes	yes	4.00	yes	yes	no
18	21.00	60.00	200.00	no	yes	2.00	•	•	•
19	1.00	2.00	15.00	no	no	2.00	no	yes	no
20	3.00	8.00	15.00	yes	no	2.00	no	yes	no
21	0	1.00	1.00	no	no	2.00	no	yes	no
22	2.00	10.00	25.00	no	no	0	yes	yes	no
23	2.00	2.00	20.00	no	no	10.00	no	yes	no
24	0	2.00	18.00	no	no	2.00	no	no	no
25	0	4.00	20.00	no	no	0	no	yes	no
26	0	7.00	35.00	no	yes	0	no	yes	no
27	2.00	6.00	45.00	no	no	0	yes	yes	no
28	0	2.00	40.00	no	yes	•	no	no	no
29	4.00	8.00	50.00	no	no	8.00	no	yes	no
30	0	4.00	•	no	no	•	no	no	no
31	4.00	4.00	17.00	no	yes	2.00	yes	yes	no
32	1.00	•	•	no	no	3.00	yes	yes	no
33	0	0	5.00	no	no	•	no	yes	no
34	0	0	0	no	yes	•	no	no	no
35	0	1.00	13.00	no	no	•	no	no	no
36	1.00	2.00	120.00	no	no	0	no	yes	no
37	0	4.00	12.00	no	no	0	no	yes	•

	PsySts	PhySts	ChgMed	CofTea	etoh	Period	Pain	Flight	TruTim
1	yes	yes	no	no	no	no	yes	Honolulu-SanFran	270.00
2	no	yes	no	no	no	no	no	SanFran-Honolulu	315.00
3	yes	yes	no	no	no	no	no	Denver-DC	480.00
4	yes	no	no	no	no	no	no	Orlando-St. Lois	140.00
5	no	no	no	no	no	no	no	DC-Atlanta	90.00
6	yes	no	no	yes	yes	no	no	DC-New Orleans	150.00
7	yes	yes	no	no	no	no	no	DC-Melbourne.Fla	150.00
8	yes	no	no	no	no	no	no	Baltimore-Pheonix	240.00
9	yes	no	no	no	no	no	no	Baltimore-S-Diego	390.00
10	no	no	no	no	no	no	no	Newark-Cincinatti	360.00
11	yes	no	no	no	no	no	no	CT-Philadelphphia	60.00
12	yes	yes	no	no	no	no	no	Cancun-SanFran	300.00
13	yes	yes	no	no	no	no	no	GBoro.NC-GBay.WI	251.00
14	yes	yes	no	no	no	yes	no	Raleigh, NC-Manila	1440.00
15	no	yes	no	no	yes	no	no	Houston-Cincinatti	135.00
16	yes	yes	no	no	no	no	no	Newark-Denver	250.00
17	yes	yes	no	no	no	yes	yes	Newark-Miami	150.00
18	•	•	•	•	•	•	•	Brazil-JFK, NY	780.00
19	no	no	no	no	no	no	no	Toronto-Great Brit.	420.00
20	yes	yes	no	no	no	no	no	LAX, CA-Tokyo	720.00
21	no	no	no	no	no	no	no	Frankfurt-LAX, CA	630.00
22	yes	yes	no	no	no	no	no	San Fran-Denmark	660.00
23	no	no	yes	no	no	no	no	Honolulu-Orlando	600.00
24	yes	no	yes	no	no	yes	no	Frankfurt-Male	525.00
25	no	yes	no	no	no	no	no	Chicago-Phoenix	180.00
26	yes	no	yes	no	yes	no	no	Honolulu-Tokyo	470.00
27	yes	no	no	no	no	no	no	Phoenix-JFK, NY	300.00
28	no	no	yes	no	no	no	no	Oakland-Baltimore	427.00
29	yes	no	no	no	yes	yes	no	Nport, VA-Chicago	139.00
30	no	no	no	no	no	no	no	Honolulu-Orlando	510.00
31	yes	no	no	yes	yes	no	no	San Fran-Honolulu	315.00
32	yes	no	yes	no	yes	yes	no	LAX, CA-Pheonix	70.00
33	yes	no	yes	no	yes	yes	no	Boston-San Fran	390.00
34	yes	no	•	•	no	no	•	HartFd.CT-Orlando	120.00
35	yes	yes	yes	no	no	•	•	Honolulu-Oregon	495.00
36	yes	no	no	no	no	yes	no	Denver-Miami	335.00
37	yes	no	no	no	no	•	no	Pittsbgh-Washton	65.00

	TZ	TThr/2	TZup4	DepCo	ArrCo	ICAO	Direct	SlpFly	BerFly	WinFly	MixFly
1	3	1.12	0	1	1	3.12	East	90.00	0	0	0
2	3	2.61	0	•	•	•	West	•	0	0	0
3	2	2.00	0	1	0	3.00	East	70.00	0	0	0
4	1	.58	0	1	2	3.58	N-S	45.00	0	0	2
5	0	.37	0	1	0	1.37	N-S	0	0	0	0
6	1	.62	0	0	4	4.62	West	0	0	0	0
7	0	.62	0	3	1	4.62	N-S	0	0	0	0
8	2	1.00	0	0	2	3.00	West	70.00	3	3	•
9	3	1.62	0	0	2	3.62	West	30.00	0	0	0
10	0	3.00	0	3	4	10.00	West	120.00	0	0	0
11	0	.25	0	3	4	7.25	West	0	0	0	0
12	2	1.25	0	3	1	5.25	N-S	0	0	0	0
13	1	2.83	0	3	4	9.83	N-S	0	0	0	0
14	11	6.00	7	0	1	14.00	West	360.00	0	6	0
15	1	.56	0	1	2	3.56	East	0	0	0	0
16	2	1.04	0	0	2	3.04	West	30.00	0	0	0
17	0	.62	0	0	4	4.62	N-S	0	0	0	0
18	2	3.25	0	0	3	6.25	N-S	360.00	0	0	0
19	5	1.75	1	3	3	8.75	East	15.00	0	0	0
20	7	3.00	3	0	4	10.00	West	45.00	0	0	0
21	9	2.62	5	0	4	11.62	West	0	0	0	0
22	9	2.75	5	0	4	11.75	East	180.00	0	0	0
23	3	2.50	0	3	2	7.50	East	90.00	0	0	0
24	4	4.25	0	3	4	11.25	East	150.00	0	0	0
25	2	1.50	0	1	2	4.50	West	0	0	0	0
26	6	4.50	2	0	4	10.50	West	120.00	0	2	0
27	2	2.50	0	0	2	4.50	East	0	0	0	0
28	3	3.06	0	0	0	3.06	East	60.00	0	0	0
29	1	1.15	0	0	4	5.15	West	0	0	0	0
30	7	4.25	3	4	4	15.25	East	60.00	0	1	0
31	3	2.62	0	0	2	4.62	West	0	0	0	0
32	1	.58	0	0	2	2.58	East	0	0	0	0
33	3	3.25	0	3	4	10.25	West	30.00	1	0	0
34	0	1.00	0	3	4	8.00	N-S	0	0	0	0
35	3	4.12	0	3	3	10.12	East	60.00	0	0	0
36	2	2.75	0	0	0	2.75	East	0	0	0	0
37	0	.50	0	3	4	7.50	East	0	0	0	0

	CofFly	CigFly	BigFud	Snack	NonAlc	Slp-7	Slp-6	Slp-5	Slp-4	Slp-3	Slp-2
1	0	0	1	1	1	7.00	6.00	8.00	8.00	6.50	7.50
2	2	0	1	1	1	•	•	•	•	•	•
3	0	0	2	1	•	•	6.00	6.00	6.00	6.00	6.00
4	0	0	1	0	•	7.00	7.00	7.00	7.00	7.00	7.00
5	0	0	1	0	•	8.00	6.50	6.00	8.00	8.50	8.50
6	1	0	0	1	•	7.00	8.00	8.00	6.50	7.50	8.00
7	0	0	0	1	•	6.00	6.00	6.00	6.00	11.00	10.00
8	2	0	1	0	•	8.00	8.00	10.00	8.50	8.00	7.00
9	0	0	1	1	•	8.00	9.00	7.00	7.00	8.00	7.00
10	2	0	2	0	•	6.50	8.00	7.00	5.50	6.00	7.00
11	1	0	0	0	•	7.00	7.00	7.00	7.00	7.00	7.00
12	3	10	1	0	•	5.00	6.00	9.00	6.00	5.00	5.00
13	0	0	•	•	•	5.00	6.00	5.00	6.00	5.00	5.00
14	11	0	7	0	•	7.00	9.00	7.00	8.00	6.00	8.00
15	0	0	0	0	•	8.00	8.00	8.50	8.00	8.00	7.50
16	0	0	2	3	•	9.50	10.00	8.00	8.50	8.50	8.50
17	2	3	1	0	•	10.00	9.00	8.00	8.00	8.00	8.00
18	0	0	2	1	•	7.00	4.00	4.00	5.00	7.00	6.00
19	5	0	2	0	2	10.25	8.75	9.25	9.00	8.75	9.75
20	1	0	2	0	1	7.00	4.50	6.00	8.00	7.00	8.00
21	4	7	0	0	2	7.00	7.00	7.00	12.00	7.00	11.00
22	0	0	3	0	•	8.00	8.00	7.00	7.00	7.00	6.00
23	0	0	1	3	•	8.00	9.00	8.00	7.00	8.00	6.00
24	0	0	3	2	10	6.50	8.50	10.50	8.50	9.50	9.50
25	2	0	2	0	0	9.00	10.00	9.00	10.00	9.00	6.00
26	1	0	2	0	•	8.00	8.00	9.00	7.00	7.25	6.50
27	0	0	1	1	2	7.00	7.50	7.50	6.00	7.00	7.00
28	0	0	1	2	4	6.50	8.00	7.50	9.50	7.00	7.00
29	2	0	1	0	0	8.50	7.00	7.00	7.50	7.25	7.50
30	0	0	1	0	0	7.25	6.50	4.75	5.25	•	3.00
31	0	0	1	1	2	8.50	8.00	8.00	9.50	10.00	9.00
32	0	0	0	0	0	8.00	7.00	8.00	8.00	7.00	8.00
33	1	0	1	1	2	9.00	9.75	8.00	7.00	6.00	6.00
34	0	0	1	0	•	8.00	9.00	9.00	10.00	9.00	9.00
35	0	0	0	1	1	10.50	10.50	10.00	12.00	3.00	•
36	0	0	1	0	•	•	•	•	•	•	•
37	1	0	0	1	•	•	•	•	•	•	•

	Slp-1	SlpDay0	Slp+1	Slp+2	Slp+3	Slp+4	Slp+5	Slp+6	Slp+7	AvPreSlp
1	6.50	7.50	7.00	6.00	7.00	6.00	8.00	6.50	7.00	7.07
2	•	2.75	6.00	6.00	•	7.00	5.00	5.00	7.00	•
3	6.00	•	6.50	6.50	5.00	6.00	6.00	6.50	5.00	6.00
4	7.00	8.00	8.00	7.00	6.00	7.00	8.00	7.00	7.00	7.00
5	8.00	6.50	8.00	7.50	7.00	8.00	8.50	8.00	7.00	7.64
6	6.00	8.50	8.00	4.00	8.00	8.50	7.50	8.00	8.00	7.28
7	6.00	5.50	11.00	10.00	6.00	6.00	6.00	6.00	6.00	7.28
8	7.00	•	8.00	8.00	8.00	8.00	7.50	•	•	8.07
9	6.00	8.00	7.00	7.00	8.00	9.50	8.00	8.00	8.00	7.42
10	4.25	7.00	6.50	7.50	6.50	7.00	8.00	7.50	6.00	6.32
11	7.00	5.50	6.00	6.50	7.75	8.00	6.50	6.00	5.50	7.00
12	5.00	4.00	6.00	5.00	5.00	5.00	6.00	6.00	5.00	5.85
13	4.00	6.50	4.00	5.00	5.00	5.00	6.00	5.00	3.00	5.14
14	6.00	5.00	9.00	8.00	10.00	9.00	6.00	•	•	6.42
15	7.00	7.00	7.00	6.00	8.00	7.00	7.50	8.00	8.00	7.85
16	8.50	7.50	9.50	8.50	9.00	7.50	9.00	9.00	9.00	8.78
17	6.00	5.50	8.00	8.00	7.00	7.50	9.00	9.00	7.50	8.14
18	0	6.00	5.00	7.00	4.00	4.00	3.00	4.00	2.00	4.71
19	9.75	10.00	8.75	10.00	10.25	10.00	9.00	7.50	9.50	9.35
20	3.00	8.00	6.50	5.50	5.50	6.00	7.00	5.75	8.00	6.21
21	11.00	0	12.00	12.00	13.00	11.00	16.00	11.00	8.00	8.42
22	6.50	3.00	9.00	8.00	8.00	10.00	3.00	6.00	6.00	7.07
23	6.00	2.00	6.00	5.00	5.00	7.00	5.00	7.00	8.00	7.42
24	9.00	7.50	9.50	8.00	8.00	7.50	8.00	7.50	7.50	8.85
25	6.50	11.50	9.00	9.00	8.00	8.00	9.00	9.00	8.00	8.50
26	5.50	2.00	12.00	8.00	7.00	12.00	7.00	7.00	5.00	7.32
27	4.00	10.00	10.00	8.00	6.00	5.00	8.00	7.50	9.00	7.00
28	7.50	7.50	5.50	9.00	6.00	9.50	10.00	9.00	9.50	7.57
29	5.00	6.50	8.00	10.00	7.50	7.75	6.00	9.00	7.75	7.03
30	4.50	2.00	8.50	10.00	7.00	7.50	7.50	6.50	9.00	5.20
31	10.00	•	•	•	•	•	•	•	•	9.00
32	0	9.00	10.00	9.00	8.00	10.00	9.00	11.00	9.00	6.57
33	5.00	6.00	7.00	6.00	9.00	9.00	9.00	•	•	7.25
34	7.50	12.50	9.00	10.00	10.00	10.00	9.00	9.00	9.00	8.78
35	11.00	4.00	10.00	10.00	9.00	8.00	11.00	10.00	9.50	10.80
36	•	8.00	8.50	8.50	9.00	8.50	9.00	8.50	8.50	•
37	•	•	•	•	•	•	•	•	•	•

	AvPstSlp	SlpLoss	Fit-7	Fit-6	Fit-5	Fit-4	Fit-3	Fit-2	Fit-1	FitDay0	Fit+1	Fit+2	Fit+3
1	6.87	-.02	0	0	0	0	0	0	0	0	0	0	0
2	5.29	•	0	0	0	0	0	0	0	0	0	0	16
3	6.08	-.08	0	0	0	0	0	0	0	0	0	0	1
4	7.28	.28	0	0	0	0	0	0	0	0	0	0	0
5	7.64	0	0	0	0	0	0	0	0	0	0	0	0
6	7.50	.22	0	0	0	0	0	0	0	0	0	0	0
7	7.21	-.07	0	0	0	0	0	0	0	0	0	0	0
8	7.90	-.17	0	0	0	0	0	0	0	0	0	0	0
9	7.92	.50	3	0	0	1	1	0	0	1	0	0	0
10	7.00	.68	2	1	0	0	0	3	0	1	2	2	0
11	6.46	-.54	0	0	0	0	0	0	0	0	0	0	0
12	5.28	-.57	0	0	0	0	0	0	0	0	0	0	0
13	5.21	.07	0	0	0	0	0	0	0	0	0	0	0
14	7.83	1.41	0	0	0	0	0	0	0	0	0	0	0
15	7.21	-.64	0	0	0	0	0	0	0	0	0	0	0
16	8.57	-.21	0	0	0	0	0	0	0	0	0	0	0
17	7.71	-.43	2	2	2	0	2	1	3	4	2	1	3
18	4.71	0	0	0	0	0	1	0	1	0	1	0	0
19	9.37	.02	0	0	0	0	0	0	0	0	0	0	0
20	6.32	.11	0	0	0	0	0	1	1	0	0	14	3
21	10.71	2.29	0	0	0	0	0	0	0	0	0	0	0
22	6.71	-.36	0	0	0	0	0	0	0	0	0	0	0
23	5.28	-2.14	0	0	0	0	0	0	0	0	0	0	1
24	8.00	-.85	0	0	0	0	0	0	0	0	0	0	0
25	9.07	.57	0	0	0	0	0	0	0	0	0	0	0
26	7.85	.53	0	0	0	0	0	0	0	0	0	0	0
27	7.78	.78	0	0	0	0	0	0	0	0	0	0	0
28	8.07	.50	0	0	0	0	0	0	0	0	1	0	0
29	7.82	.79	0	0	0	0	0	0	0	0	0	0	0
30	7.00	1.80	0	0	0	0	0	0	0	0	0	0	0
31	•	•	0	0	0	0	0	0	0	0	0	0	0
32	9.42	2.85	0	0	0	0	0	0	0	0	0	0	0
33	7.66	.41	0	0	1	1	1	1	0	1	1	0	0
34	9.92	1.14	4	0	0	0	1	0	0	15	0	0	2
35	8.85	-1.95	0	1	0	0	0	0	1	0	0	0	0
36	8.57	•	0	0	0	0	0	0	0	0	0	0	0
37	•	•	0	0	0	0	0	0	0	0	0	0	0

	Fit+4	Fit+5	Fit+6	Fit+7	mean pre fit	mean post fit	sum sz pre	sum sz post
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	2.00	0	16
3	2	0	0	0	0	.38	0	3
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0
9	0	0	0	0	.71	.12	5	1
10	0	1	0	1	.86	.88	6	7
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0
14	0	3	0	0	0	.38	0	3
15	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0
17	2	0	2	3	1.71	2.13	12	17
18	1	0	0	0	.29	.25	2	2
19	0	0	0	0	0	0	0	0
20	3	3	4	5	.29	4.00	2	32
21	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0
23	0	0	0	1	0	.25	0	2
24	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0
28	0	0	0	0	0	.13	0	1
29	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0
31	0	1	0	0	0	.13	0	1
32	0	0	0	0	0	0	0	0
33	0	0	0	0	.57	.25	4	2
34	0	1	0	0	.71	2.25	5	18
35	0	0	0	0	.25	0	2	0
36	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0

	sz mean diff	sum sz diff	1/x Fit/mth + 1	distance	1/x mean sz diff + 1
1	0	0	.77	2091	1.00
2	2.00	16	.14	2091	.33
3	.38	3	.67	1473	.73
4	0	0	.67	904	1.00
5	0	0	1.00	496	1.00
6	0	0	.89	918	1.00
7	0	0	1.00	835	1.00
8	0	0	.50	1977	1.00
9	-.58	-4	1.00	2271	2.38
10	.02	1	.11	557	.98
11	0	0	1.00	136	1.00
12	0	0	.81	2423	1.00
13	0	0	1.00	753	1.00
14	.38	3	.67	9746	.72
15	0	0	1.00	915	1.00
16	0	0	1.00	1619	1.00
17	.42	5	.08	1072	.70
18	-.04	0	.33	4839	1.04
19	0	0	1.00	3555	1.00
20	3.71	30	.17	5492	.21
21	0	0	.20	5796	1.00
22	0	0	.89	5472	1.00
23	.25	2	.40	4754	.80
24	0	0	.15	4941	1.00
25	0	0	.93	1434	1.00
26	0	0	.25	3852	1.00
27	0	0	1.00	2160	1.00
28	.13	1	.50	2647	.88
29	0	0	.56	710	1.00
30	0	0	1.00	4717	1.00
31	.13	1	.67	2091	.88
32	0	0	.75	351	1.00
33	-.32	-2	.11	2700	1.47
34	1.54	13	.02	1019	.39
35	-.29	-2	•	589	1.41
36	0	0	.50	1718	1.00
37	0	0	.50	169	1.00

REFERENCES

Aird, R. B. (1988). The importance of seizure-inducing factors in youth. Brain & Development, 10, 73-76.

Ames, F. (1982). The evoked epilepsies. South African Medical Journal, 61, 661-662.

Andermann, F. (1987). Identification of candidates for surgical treatment of epilepsy. In: J. Jr. Engel (Ed.), Surgical treatment of the epilepsies. (pp. 51-70). New York: Raven Press, 51-70.

Angelieri, F. (1975). Partial epilepsies and nocturnal sleep. In: P. Levin & W. P. Koella (Ed.s), Sleep, (pp. 196-203). New York: Raven Press.

Angyan, L., Katjtar, P., & Sik, E. (1967). Correlation between thalamic induced cortical spike and wave activity and behavior in unrestrained acts. Acta Physiology Academic Science, 32, 291-306.

Arias, L. P., & Passouant, P. (1971). Etude des decharges epileptigue au cours du sommeil rapide. C. R. Social Biol., 165, 1385-1389.

Ascoff, J., Hoffman, K., Pohl, H. & Wever, R. (1975). Re-entrainment of circadian rhythms after phase shifts of the zeitgeber. Chronobiologia, 2, 23-78.

Baldy-Moulinier, M. (1982). Temporal lobe epilepsy and sleep organization. In: Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and Epilepsy. (pp. 347-359). New York: Academic Press.

Bechinger, D., & Kornhuber, H. H. (1976). The sleep deprivation EEG in childhood. Electroencephalography and Clinical Neurophysiology, 41, 654.

Bechinger, D., Kriebel, J., & Schlager, M. (1973). Das schlafentzugs-EEG, ein wichtiges diagnostisches hilsmittel bei cerebralen anfällen. Z. Neurlogie, 205, 194-206.

Bekhtereva, N. P, Kambarova, D. K., & Pozdeev, V. K. (1978). The stable pathological state in brain diseases, Meditsina, 8, 11-21.

Bennett, D. R., Ziter, F. A., & Liske, E. A. (1969). Electroencephalographic study of sleep deprivation in flying personnel. Neurology, 19, 375-377.

Bergonza, P., Chiurulla, C., & Cianchetti, C. (1972). Deprivation of the fourth sleep phase of epileptics. Neurology, 42, 506-512.

Berti-Ceroni, G., Sabattini, L., Gambi, D., & Lugaresi, E. (1967). Effects of sleep deprivation in epileptics. Neurology, 37, 305-320.

Besset, A. Influence of generalized seizures on sleep organization. In: M. B. Sterman, M. N. Shouse & P. Passouant (Eds.), Sleep and Epilepsy, (pp. 339-346), New York: Academic Press.

Billiard, M. (1982). Epilepsies and the sleep-wake cycle. In M. P. Sterman, M. N. Shouse, & P. Passouant (Eds.) Sleep and Epilepsy. New York: Academic Press, 269-286.

Biniaurishvili, R. G., & Yakhno, N. N. (1982). Electroencephalographic features of slow sleep in epilepsy. Human Physiology, 8, 396-402.

Birbaumer, N., Lutzenberger, W., Elbert, T., & Trevorrow, T. (1992). Threshold variations in cortical cell assemblies and behavior. In: H. J. Heinze (Eds.), New developments in event-related potentials. Boston: Birkhäuse

Bittner-Manicka, M. (1976). Investigations on the mechanism of nocturnal epilepsy. Journal of Neurology, 211, 169-181.

Bowersox, S. S. & Drucker-Colin, R. (1982). Seizure modification by sleep deprivation: a possible protein synthesis mechanism. In Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and Epilepsy. (pp. 94-104). New York: Academic Press.

Bremer, F. (1975). Existance of a mutual tonic inhibitory interaction between the preoptic hypnogogic structure and the midbrain reticular formation. Brain Research, 96, 71-75.

Bridgers, S. L., & Ebersole, J. S. (1987). Supervision of ambulatory cassette EEG screening: a strategy based on the temporal distribution of epileptiform abnormalities, Electroencephalography and Clinical Neurophysiology, 66, 219-224.

Broughton, R. J. (1978). Sleep and epilepsy. In: Epilepsy. (pp. 57-62). London: British Epilepsy Association.

Buck, A., Tobler, I., & Borbely, A. A. (1989). Wrist activity monitoring in air crew members: a method for analyzing sleep quality following transmeridian and north-south flights. Journal of Biological Rhythms, 4, 93-105.

Bureau, N., Guey, J., & Dravet, C. (1968). A study of the distribution of the petit mal absences in the child in relation to his activities. Electroencephalography and Clinical Neurophysiology, 25, 513.

Cadilhac, J. (1982). Complex partial seizures and REM sleep. In Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and Epilepsy. (pp. 315-324). New York: Academic Press.

Caesar, H. (1986). Long-term statistics and their impact on safety management and operational procedures. Proceedings of the 39th International Air Safety Seminar. Arlington, VA: Flight Safety Foundation. 11-23.

Carruthers, M., Arguelles, A. E., & Mosovich, A. (1976). Man in transit: Biochemical and physiological changes during intercontinental flights. Lancet, 1, 977-980.

Cohen, H. B., & Dement, W. C. (1965). Sleep: Changes in threshold to convulsive shock in rats after deprivation of "paradoxical" phase. Science, 150, 1318.

Colin, J., Timbal, J., Boutelier, C., Houda, Y., & Siffre, M. (1968). Rhythm of the rectal temperature during a 6-month free-running experiment. Journal of Applied Physiology, 25, 170-176.

Corliss, C. J. (1949). The day of the two noons. Washington, D.C.: Association of American Railroads.

Czeisler, C. A., Weitzman, E. D., Moore-Ede, M. C., Zimmerman, J. C., & Knauer, R. S. (1980). Human sleep: Its duration and organization depend on its circadian phase. Science, 210, 1264-1267.

Da Silva, A. M., Aarts, J. H., Binnie, C. D., Laxminarayan, R., Lopes Da Silva, F. H., Meijer, J. W., & Nagelkerke, N. (1984). The circadian rhythm of interictal epileptiform EEG activity. Electroencephalography and Clinical Neurophysiology, 58, 1-13.

Dahl, J., Melin, L., Brorson, L. & Schollin, J. (1985). Effects of a broad-spectrum behaviour modification treatment programme on children with refractory epileptic seizures. Epilepsia, 26, 303-309.

Dahl, J., Melin, L., & Lund, L. (1987). Effects of a contingent relaxation treatment programme on adults with refractory epileptic seizures. Epilepsia, 28, 125-137.

D'Alessandro R., Sintini, M., Pazzaglia, P., & Lugaresi, E. (1983). Pure sleep epilepsies: Prognostic features. In: Epilepsy: An update on research and therapy. (pp. 235-239). New York: Alan R. Liss.

Dalessio, D. J. (1985). Seizure disorders and pregnancy. New England Journal of Medicine, 312, 559-563.

Declerk, A. C., Wauquier, A., Sijben-Kiggen, R., & Martens, W. (1982). A normative study of sleep in different forms of epilepsy. In: M. B. Sterman, M. N. Shouse, & P. Passouant (Eds.), Sleep and epilepsy. (pp. 329-337). New York: Academic Press.

Degen, R. (1980). A study of the diagnostic value of resting and sleep EEG's after sleep deprivation in epileptic patients on anticonvulsive therapy. Electroencephalography and Clinical Neurophysiology, 49, 577-584.

Delange, M., Castan, P., Cadilhac, J., & Passouant, P. (1962). Study of night sleep during centrencephalic and temporal epilepsies. Electroencephalography and Clinical Neurophysiology, 14, 777.

Dement, W. C., Seidel, W. F., Cohen, S. A., Bliwise, N. G., Carskadon, M. A. (1986). Sleep and wakefulness in aircrew before and after transoceanic flights. Aviation Space and Environmental Medicine, 57, 12, 14-28.

Efron, R. (1956). Effects of olfactory stimuli in arresting uncinate fits. Brain, 79, 267.

Elbert, T., Rockstroh, B., Canavan, T., Birbaumer, N., Lutzenberger, W., Von Bülow, I., & Linden, A. (1991). Self-regulation of slow cortical potentials and its role in epileptogenesis. In: J. G. Carlson, & A. R. Seifert (Eds.), International Perspectives on Self-Regulation and Health. (pp. 65-94). New York: Plenum Press.

Ehret, C. F., & Scanlon, L. W. (1983). Overcoming jetlag. New York: Berkley.

Elwes, R. D., Johnson, A. L., Shorvon, S. D., Reynold, E. H. (1984). The prognosis for seizure control in the newly diagnosed epilepsy. New England Journal of Medicine, 311, 944-947.

Epstein, A. W. & Hill, W. (1966). Ictal phenomena during REM sleep of a temporal lobe epileptic. Archives of Neurology, 15, 367-375.

Feeney, D. M., & Gullotta, F. P. (1972). Supression of seizure discharges and sleep spindles by lesions of the rostral thalamus. Brain Research, 45, 254-259.

Feldman, B. G., & Paul, N. G. (1976). Identity of emotional triggers in epilepsy. Journal of Nervous and Mental Disease, 162, 345-352.

Fenwick, P. B. (1990). Behavioral treatment of epilepsy. Postgraduate Medical Journal, 66, 336-338.

Fenwick, P. B. (1991). Evocation and inhibition of seizures: Behavioral Treatment. In: D. Smith, D. Treiman, & M. Trimble (Eds.), Advances in Neurology, (pp.163-183). New York: Raven Press, Ltd.

Fere, C. (1890) Les Epilepsies et les Epileptigues. Paris, Alcan.

Forster, F. (1969). Conditional reflexes and sensory evoked epilepsy: The nature of the therapeutic process. Conditional Reflex, 4, 103-114.

Forster, F. M. (1972). Classification and conditioning treatment of the reflex epilepsies. International Journal of Neurology, 9, 73-86.

Frank, G. S. & Pegrani, G. V. (1974). Interrelations of sleep and focal epileptiform discharge in monkeys with alumina cream lesions. Aeromedical Research Laboratories Publications, ARL-TR-70-12: 27.

Gander, P. H., Myhre, G., Graeber, R. C., Anderson, H. T., & Lauber, J. K. (1985). Crew factors in flight operations: I. Effects of 9-hour time-zone changes on fatigue and the circadian rhythms of sleep/wake and core temperature (NASA Technical memorandum 88197). Moffett Field, CA: NASA-Ames Research Center.

Gastaut, H. & Broughton, R. A. (1965). A clinical and polygraphic study of episodic phenomena during sleep. In: J. Wortis (Ed.), Recent Advances in Biological Psychiatry, 7, 197-221. New York: Plenum Press.

Gabor, A., & Seyal, M. (1986). Effect of sleep on the electroencephalographic manifestations of epilepsy. Journal of Clinical Neurophysiology, 3, 23-38.

Ghata, J., Fourn, F., & Borrey. (1967). Application de l'etude des variations circadiennes à l'analyse des vois comportant le passage de fuseaux horaires. Paper presented at the 16th International Congress of Aviation and Space medicine, Lisbon.

Gibbs, F. A., & Gibbs, E. L. (1947). Diagnostic and localisating value of EEG studies in sleep. Research Publication of Nervous and Mental Disorders, 26, 366-376.

Gibbs, F. A., & Gibbs, E. L. (1952). Atlas of electroencephalography. Vol. II. Cambridge, Mass: Addison-Wesley Press.

Gibberd, F. B., & Bateson, M. C. (1974). Sleep epilepsy: Its pattern and prognosis. British Medical Journal, 2, 403-405.

Gowers, W. R. (1885). Epilepsy and other chronic convulsive diseases. London: William Wood & Co.

Graeber, R. C. (1982). Alterations in performance following rapid transmeridian flight. In F. M. Brown & R. C. Graeber (Eds.), Rhythmic aspects of behavior (pp. 173-212). Hillsdale, NJ: Erlbaum.

Graeber, R. C. (1988). Aircrew fatigue and circadian rhythmicity. Human factors in aviation. New York: Academic Press, Inc.

Graeber, R. C., Dement, W. C., Nicholson, A. N., Sasaki, M., & Wegmann, H. M. (1986). International cooperative study of aircrew layover sleep: Operational summary. Aviation, Space and Environmental Medicine, 57 (Suppl. 12), B10-B13.

Graeber, R. C., Lauber, J. K., Connell, L. J., and Gander, P. H. (1986). International aircrew sleep and wakefulness after multiple time zone flights: A cooperative study. Aviation, Space, and Environmental Medicine, 57, B3-B9.

Graybeal, N. L. (1991). A report on the epilepsy population in Hawaii. Honolulu: Author

Guerroro-Figureoa, R., Barros, A., & De Balbian-Vester, F. (1963). some inhibitory effects of attentive factors on experimental epilepsy. Epilepsia, 4, 225-240.

Gumnit, R. J. (1987). Postscript: Who should be referred for surgery? In: J. Jr. Engel (Ed.), Surgical treatment of the epilepsies. (pp. 71-74). New York: Raven Press.

Gunderson, M. C., Dunne, P. B., & Feyer, T. L. (1973). Sleep deprivation seizures. Neurology, 23, 678-686.

Halasz, P. (1982). Generalized epilepsy with spike-wave pattern and intermediate states of sleep. In Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and epilepsy. (219-238). New York: Academic Press.

Hamel, A. R. & Sterman, M. B. (1982) Sleep and epileptic abnormalities during sleep. In Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and epilepsy. (pp. 361-377). New York: Academic Press.

Hauri, P. (1982). The sleep disorders. Kalamazoo, Michigan: Upjohn.

Hauser, W. A., Hesdorffer, D. C. (1990). Epilepsy: Frequency, causes and consequences. New York: Demos.

Hauty, G. T. (1966). Life sciences and space research. Aerospace Medicine, 37, 668.

Hauty, G. T., & Adams, T. (1966). Phase shifts of the circadian system and performance deficit during the periods of transition: II. West-east flight. Aerospace Medicine 37: 1027-1033.

Heinemann, L. G. (1966). Der mehrtägige Schlafentzug in der experimentellen Psychoseforschung: Psychopathologie und EEG. Archives Psychiatrie Nervenkronical, 214, 177-197.

Hess, R. (1974). Sleep activation of the EEG in patients with partial seizures. In: H. M. Van Praag & H. Meinardi (Eds.), Brain and sleep. (pp. 140-153). Amsterdam: De Erven Bohn.

Hess, W. R. (1954). The diencephalic sleep center. In: J. F. Sela Fresnaye (Ed.), Brain mechanisms and consciousness symposium. (pp. 130) Oxford: Blackwell.

Hoeppner, J. B., Garron, D. C., & Cartwright, R. D. (1984). Self-reported sleep disorder symptoms in epilepsy, Epilepsia, 25, 434-437.

Hoffman, K. (1965) Circadian clocks, J. Aschoff (Ed.) Amsterdam: North-Holland.

Hopkins, H. (1933). The time of appearance of epileptic seizures in relation to age, duration and type of syndrome. Journal of Nervous and Mental Disorders, 77, 153-162.

Ingvar, D. H. (1955). Reproduction of the three per second spike-wave EEG pattern by subcortical electrical stimulation in cats. Acta Physiologica Scandanavia, 33, 1-14.

Jackson, J. H. (1931). On epilepsy and epileptiform convulsion. In: Selected writings, Volume I, J. Taylor (ed.). London: Staples Press.

Janz, D. (1962). The grand mal epilepsies and the sleep-wake cycle. Epilepsia, 3, 69-109.

Jasper, H. H., & Droogleever-Fortuyn, J. (1947). Experimental studies on the functional anatomy of petit mal epilepsy. Research Assessment of Nervous Development, 26, 272-298.

Johnson, L. C. (1969). Psychological and physiological changes following total sleep deprivation. In A. Kales (Ed.), Sleep: Physiology & Pathology, (pp. 206). Philadelphia: Lippincott.

Jones, H. S., & Oswald, I. (1968). Two cases of healthy insomnia. Electroencephalography and Clinical Neurophysiology, 24, 378.

Jouvet, M. (1969). Biogenic amines and the states of sleep. Science, 163, 32-41.

Jovanovic, U. J. (1967). Das schlafverhalten des epileptikers. II. elemente des EEGs, vegetativum und motorik. Dt. Z. NervHeilk, 191, 257-290.

Junko, M. F., Andy, V. J., & Webster, C. L. (1971). Disordered sleep patterns following thalamotomy. Clinical Electroencephalography, 2, 213-217.

Jung, R. (1954). Correlations of bioelectrical and arousal in man. In: J.F. De La Fresnaye (Ed.) Brain mechanisms and consciousness. (pp. 310-344.) Oxford: Blackwell.

Kellaway, P. (1985). Sleep and Epilepsy. Epilepsia, 26, S15-S30.

Kellaway, P., Frost, Jr., J. D., & Crawley, J. M. (1980). Time modulation of spike-and-wave activity in generalized epilepsy. Annals of Neurology, 8, 491-500.

Kikuchi, S. (1969). An electroencephalographic study of nocturnal sleep in temporal lobe epilepsy. Folia Psychiatria Neurologica Japan, 23, 59-81.

Klein, K. E., Brüner, S., Kuklinski, P., Ruff, S., & Wegmann, H. M. (1972). The evaluation of studies of flight personnel of the German Lufthansa on the question of stress during flights on the short European routes. NASA Technical Memorandum 76660, 1982, Washington, DC: NASA.

Klein, K. E., Brüner, S., & Ruff, Z. (1968). Aerospace Medicine, 39, 512.

Klein, K. E., Wegmann, H. M., & Hunt, B. I. (1972b.). Desynchonization of body temperature and performance circadian rhythm as a result of outgoing and homegoing transmeridian flights, Aerospace Medicine, 43, 119-132.

Klein, K. E., & Wegmann, H. M. (1980). Significance of circadian rhythms in aerospace operations (NATO AGARDograph No. 247). Neuilly sur Seine: NATO AGARD.

Knowles, J. B., Laverty, S. G., & Kuechler, H. A. (1968). Effects of alcohol on REM sleep. Quarterly Journal of Studies on Alcohol, 29, 342-349.

Kravtsov, A. (1967). Official letter from the Ministry of Civil Aviation, U.S.S.R., to the U.S. Federal Aviation Agency.

Labar, D. R. (1992). Seizure disorders. In: R. Berkow, & A. J. Fletcher (Eds.), The Merck manual.16th Edition. (pp.1436). Rahway, New Jersey: Merck & Co., Inc.

Langdon-Down, M. & Brain, W. R. (1929). Time of day in relation to convulsions in epilepsy. Lancet, 2, 1029-1032.

Laverdiere, M., Montplaisir, J., & Saint-Hilaire, J. M. (1984). Nocturnal seizures and sleep in patients studied with depth electrodes. Sleep Research, 13, 178.

Lennox, W. G., Gibbs, F. A., & Gibbs, E. L. (1936). Effect on the electroencephalogram of drugs and conditions which influence seizures. Archives of Neurological Psychiatry, 36, 1236-1245.

Lennox, G. M. (1955). In Cecil R. L., & Loeb, R. F. (ed.s) Texbook of medicine. (pp. 1494). Philadelphia: Saunders Company.

Lewy, F. M., & Gammon, G. D. (1940). Influence of sensory systems on spontaneous activity of cerebral cortex. Journal of Neurophysiology. 3, 388-395.

Lieb, J., Joseph, J. P., Engel, J., & Crandal, R. (1980). Sleep state and seizure foci related to depth spike activity in patients with temporal lobe epilepsy. Electroencephalography and Clinical Neurophysiology, 49, 538-557.

Lockard, J. S. (1980). A primate model of clinical epilepsy: mechanisms of action through quantification of therapeutic effects. In: J. S. Lockard, & A. A. Ward (Eds.), Epilepsy: A window to brain mechanisms. New York: Raven Press.

Loomis, A. L., Harvey, N., & Hobart, G. A. (1937). Cerebral states during sleep as studied by human brain potentials. Journal of Experimental Psychology, 21, 127-144.

Lyman, E. G., & Orlady, H. W. (1980). Fatigue and associated performance decrements in air transport operations. Final report: NASA Contract NAS2-10060. Moffett Field, CA: NASA-Ames Research Center.

Luce, G. G. (1971). Body time. New York: Panteon Books.

Madoz, P., & Reinoso-Suarez, F. (1968). Influences of lesions in preoptic region on state of sleep and wakefulness. Proceedings of 24th International Congress of Physiological Sciences, Washington, 827.

Mattson, R. H., Cramer, J. A., Collins, J. F., et al. (1985). Comparison of carbamazepine, phenobarbital, phenotoin, and primidone in partial and secondary generalized tonic-clonic seizures. New England Journal of Medicine, 313, 145-151.

Mattson, R. H., Pratt, K. L., & Calverley, J. R. (1965). Electroencephalograms of epileptics following sleep deprivation. Archives of Neurology, 13, 310-315.

Mayanagi, Y. (1977). The influence of natural sleep on focal spiking in experimental temporal lobe epilepsy in the monkey. Electroencephalography and Clinical Neurophysiology, 43, 813-824.

Mayersdorf, A. & Wilder, B. J. (1974). Focal epileptic discharges during all night sleep studies. Clinical Electroencephalography, 5, 73-87.

McGinty, D. J., & Sterman, M. B. (1968). Sleep suppression after basal forebrain lesion in the cat. Science, 160, 1253-1255.

McFarland, R. A. (1941). Fatigue in aircraft pilots. New England Journal of Medicine, 225, 845-855.

Meddis, R., Pearson, A. J. D., & Langford, G. (1973). An extreme case of healthy insomnia. Electroencephalography and Clinical Neurophysiology, 35, 213.

Menzel, W. (1962). Mensliche tag-nacht rhythmic und schichtarbeit. Basel, Switzerland: Benno Schwabe.

Merritt, H. H. (1967). Texbook of neurology. Philadephia: Lea & Febiger.

Miles, L. E., & Dement, W. C. (1980). Sleep-wake complaints of elderly men and women. Sleep, 3, 121-129.

Milton, J. G., Gotman, J., & Remillard, G. M. (1987). Timing of seizure recurrence inadult epileptic patients: a statistical analysis. Epilepsia, 28, 471-478.

Minors, D. S., & Waterhouse, J. M. (1981). Circadian rhythm and the human. Bristol: John Wright & Sons Ltd.

Moore-Ede, M., Sulzman, F., & Fuller, C. (1982). The clocks that time us. Cambridge: Harvard University Press.

Montplaisir, J., Saint-Hilaire, J. M., Laverdiere, M., Walsh, J., & Bouvier, G. (1980). Contributions of all-night polygraphic recording to the localization of primary epileptic foci. In: R. Canger, F., Angeleri. and J. K. Penry (Eds.), Advances in epileptology. 11th Epilepsy International Symposium.(pp. 135-138). New York: Raven Press.

Montplaisir, J., Laverdiere. M., Saint-Hilaire, J. M. (1982). Sleep and focal epilepsy: contribution of depth recording. In Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and epilepsy. (pp. 301-314). New York: Academic Press.

Moruzzi, G. (1972). The sleep-wake cycle. Physiology, 64, 1-165.

Mullaney, D. J., Kripke, D. F., Fleck, P. A., & Johnson, L. C. (1983). Sleep loss and nap effects on sustained continuous performance. Psychophysiology, 20, 643-651.

Naitoh, P., & Dement, W. (1975). Sleep deprivation in humans. Clinical Neurophysiology, 7, 46-51.

Naitoh, P., Kales, A., Kollar, E. J., Smith, J. C., Jacobson, A. (1969). Electroencephalographic activity after prolonged sleep loss. Electroencephalography and Clinical Neurophysiology, 27, 2-11.

Neill, J. C., & Alvarez, N. (1989). The effects of the everyday environment on epileptic activity in three mentally retarded individuals. Electroencephalography and Clinical Neurophysiology, 72, 198-206.

Neugebauer, R. (1989). Reliability of seizure diaries in adult epileptic patients. Neuroepidemiology, 8, 228-233.

Nicholson, A. N. (1972). Duty hours and sleep patterns in aircrews operation world-wide routes. Aerospace Medicine, 43, 138-141.

Nicholson, A. N., Pascoe, P. A., Spencer, M. B., Stone, B. M., & Green, R. L. (1986). Nocturnal Sleep and daytime alertness of aircrew after transmeridian flights. Aviation, Space and Environmental Medicine, 57 (Suppl. 12), B43-B52.

Nicholson, A. N., Pascoe, P. A., Roehrs, T., Roth, T., Spencer, M. B. & Zorick, F. (1985). Sustained performance with short evening and morning sleeps. Aviation, Space, and Environmental Medicine, 56, 105-114.

Niedermeyer, E. (1965). Sleep electroencephalograms in petit-mal. Archives of Neurology, 12, 625-630.

Niedermeyer, E. (1972). The generalized epilepsies. New York: Plenum

Niedermeyer, E. (1990). The epilepsies: diagnosis and management. Baltimore-Munich: Urban & Schwarzenberg.

Oswald, I. (1969). Human brain proteins, drugs and dreams. Nature, 223, 893-897.

Passouant, P. (1967). Epilepsie revue. Revue Roumaine de Neurologie, 4, 151.

Passouant, P. (1982) Historical views on sleep and epilepsy. In: Sterman M. P., Shouse, M.N., & Passouant, P. (Eds.) Sleep and epilepsy. (pp. 1-9). New York: Academic Press.

Passouant, P., Cadillac, J., & Delange, M. (1965). Indications apportées par l'étude du sommeil de nuit sur la physiopathologie des épilepsies. International Journal of Neurology, 5, 207-216.

Patry, F. L. (1931). The relation of time of day, sleep and other factors to the incidence of epileptic seizures. American Journal of Psychiatry, 87, 789-813.

Patry, G., Lyagoubi, S., & Tassinari, C. A. (1971). Subclinical electrical status epilepticus induced by sleep in children. Archives of Neurology, 24, 242-252.

Penry, K., & Rachel, R. E. (1986). Epilepsy: diagnosis, management, quality of life. New York: Raven Press.

Perria, L., Rosadini, G., Rossi, G. F. & Gentilomo, A. (1966). Neurosurgical aspects of epilepsy: Physiological sleep as a means for focalizing EEG epileptic discharges. Acta Neurologica. 14, 1-9.

Pollen, D. A., Pero, P. H., & Reid, K. H. (1963). Experimental bilateral spike-and-wave from thalamic stimulation in relation to level of arousal. Electroencephalography and Clinical Neurophysiology, 15, 1017-1028.

Pompeiano, O. (1969). Sleep mechanisms. In J. Jasper, T. Ward, & T. Pope (Eds.) Basic mechanisms of the epilepsies (pp. 453-473). Boston: Little-Brown.

Porter, R. G. (1984). Epilepsy—100 elementary principles. major problems in neurology, series 12. Eastbourne: Sanders.

Post, W., & Gatty, H. (1931). Around the world in eight days. London: Hamilton.

Pratt, K. L., Mattson, R. H., Weikers, N. J., & Williams, R. (1968). EEG activiation of epilepstics following sleep deprivation: a prospective study of 114 cases. Electroencephalography and Clinical Neurophysiology, 24, 11-15.

Preston, F. S. (1973). Further sleep problems in airline pilot world-wide schedules. Aerospace Medicine, 44, 775-782.

Richardson, G. S., Carscadon, M. A., Orav, E. J., & Dement, W. C. (1982). Circadian variation in sleep tendency in elderly and young subjects. Sleep, 5 (Suppl. 2). s82-s94.

Rodin, E., Luby, E., & Gottlieb, J. (1962). The electroencephalogram during prolonged experimental sleep deprivation. EEG Clinical Neurophysiology, 14, 544.

Ross, J. J., Johnson, L. C., & Walter, R. D. (1966). Spike-and-wave discharges during stages of sleep. Archives of Neurology, 14, 399-407.

Rumpl, E., Lorenzi, E., Bauer, G., & Henge, W. (1977). Zum diagnostischen wert des EEGs nach schlafentzug. EEG-EMG, 8, 205-209.

Samel, A., & Wegmann, H. M. (1989). Circadian rhythm, sleep, and fatigue in aircrews operating on long-haul routes. In: R. S. Jensen (Ed.), Aviation Psychology. Tiptree, Essex.: Anchor Press Ltd.

Sampson, H. (1965). Deprivation of dreaming sleep by two methods. I. Compensatory REM time. Archives of General Psychiatry, 13, 79.

Sasaki, T. (1964). Proceedings of the Society of Experimental Biology and Medicine, 115, 1129.

Sasaki, M., Kurosaki, Y., Mori, A., & Endo, S. (1986). Patterns of sleep wakefulness before and after transmeridian flights. Sleep Research, 16, 645.

Scheuer, M. L. (1991). The medical patient with epilepsy. In: S. R. Resor, & H. Kutt (Eds.), Medical treatment of epilepsy. (pp. 59-72). New York: Marcel Dekker.

Scollo-Lavizzari, G., Pralle, W., & Radue, E. W. (1977). Comparative study of efficacy of waking and sleep recordings following sleep deprivation as an activation method in the diagnosis of epilepsy. European Neurology, 15, 121-123.

Selbach, H. (1962). Sleep-wake: A reciprical induction regulation model. Annals of New York Academy of Science, 98, 1221.

Siegel, P. V., Gerathewohl, S. J., & Mohler, S. R. (1969). Time-zone effects: disruption of circadian rhythms poses a stress on the long-distance air traveler. Science, 164, 1249-1255.

Solberger, A. (1966). Biological rythm research. Amsterdam: Elsevier Publishing Co.

Speckmann, E. J. & Caspers, H. (1973). Neuropsysiologische Grundlagen der Provokationsmethoden in der Elektroenzephalographhie. II. EEG-EMG, 4, 157-167.

Spunt, A. L., Hermann, B. P., & Rousseau, A. M. (1986). Epilepsy. In: M. Hersen (Ed.), Pharmacological and behavioral treatment: an integrative approach. New York: Wiley.

Strengers, T., & Esser, T. (1967). The behavior of the circadian rhythm in water and electrolyte excretion before, during and after a flight from Ameterdam to Anchorage and Tokyo. Paper presented at the 16th International Congress of Aviation and Space Medicine, Lisbon.

Sterman, M. P. (1973). Neurophysiologic and clinical studies of sensorimotor EEG biofeedback training: some effects on epilepsy. Seminars in Psychiatry, 5, 507-525.

Sterman, M. B. (1984). The role of sensorimotor rhythmic EEG activity in the etiology and treatment of gemneralized motor seizures. In T. Elbert, B. Rockstroh, W. Lutzenberger, & N. Birbaumer (Eds.), Self-regulation of the brain and behavior, (pp. 95-106). Berlin/Heidelberg: Springer.

Sterman M. P., Shouse, M.N., & Passouant, P. (1982). Diagnostic procedures employing sleep: overview. In: M. P. Sterman, M. N. Shouse, & P. Passouant (Eds.) Sleep and epilepsy. (pp. 431-432). New York: Academic Press.

Suvanto, S., Partinen, T., Harma, T., & Ilmarinen, J. (1987). Disturbances in sleep-wakefulness cycle of flight attendants after transmeridian flights. Sleep Research, 16, 645.

Tartara, A., Moglia, A., Manni, R., & Corbellini, C. (1980). EEG findings and sleep deprivation. European Neurology, 19, 330-334.

Testa, G., & Gloor, P. (1975). Generalized penicillin epilepsy in the cat: effect of midbrain cooling. Electroencephalography and Clinical Neurophysiology, 36, 517-524.

Tukey, J. W. (1977). Exploratory Data Analysis. Reading, Massachusetts: Addison-Wesley.

U.S. Bureau of the Census, Statistical Abstract of the United States: 1991 (11th edition.) Washington, DC, 1991

Vieth, J. (1986). Vigilance, Sleep and Epilepsy. European Neurology, 25, 128-133.

Villablanca, J., Schlag, J., & Marcus, R. (1970). Blocking of experimental spike-and-wave by a localized forebrain lesion. Epilepsia, 11, 163-177.

Webb, W. B., & Agnew, H. W. Jr., (1965). Sleep: Effects of a restricted regime. Science, 150, 1745.

Weitzman, E. D., Kripke, D. F., Goldmacher, D., McGregor, P., & Nogeire, C. (1970). Acute reversal of the sleep-waking cycle in man. Archives of Neurology, 22, 483-489.

Whitman, S., Coleman, T., Berg, B., King, L., & Desai, B. (1980). Epidemiological insights into the socioeconomic correlates of epilepsy. In B.P. Hermann (Ed.), A multidisciplinary handbook of epilepsy. Springfield, Ill: Thomas.

Wever, R. A. (1979). The circadian system of man. New York: Springer Verlag.

Wyler, A. R. (1974). Epileptic neurons during sleep and wakefulness. Experimental Neurology, 42, 593-608.

Zlutnick, S., Mayville, W., & Moffat, S. (1975). Behavioral control of seizure disorders: the interruption of chained behavior. In: R. C. Katz, S. Zlutnick (Eds.), Behavior therapy and health care. (pp. 317-336). New York: Pergamon Press.

Zulley, J., Wever, R., & Aschoff, J. (1981). The dependence of onset and duration of sleep on the circadian rhythm of rectal temperature. Pfluegers Archives, 391, 314-318.