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THE EFFECTS OF HIGH VERSUS LOW AMPLITUDE TRAINING OF 9-13 HERTZ EEG ACTIVITY ON THE SEIZURE RATE OF REFRACTORY EPILEPTICS

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THESIS
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Literature Review

Classifications of Epilepsy

For centuries man has tried to understand and control a variety of "mysterious disorders" that today are called epilepsy. There is not one epilepsy but rather a number of epilepsies with each exhibiting slightly different symptomatology.

Three major epilepsies exist: tonic-clonic; absence; and complex-partial (Gallagher, 1977). Tonic-clonic seizures are the result of a sudden bilateral, generalized or non-focal autonomic discharge of neurons in the cerebral cortex. During the seizure or ictal event the neural activity is characterized by bilateral grossly synchronous and symmetrical discharges of the neurons. These neural events have a duration of 1-2 minutes and result in the epileptic losing full consciousness and body tone. Following loss of consciousness, the tonic phase commences when the body becomes tense and rigid. This is followed by muscle spasms and jerks, in the myoclonic phase. Due to the motor involvement, these seizures are sometimes classified as major motor seizures. As the neural activity returns to normal, the body relaxes, however, the person remains unconscious for several minutes. Upon awakening the epileptic feels tired, sleepy and disoriented. Amnesia usually occurs for the ictal and post ictal events (Gallagher, 1977).
Absence is a non-convulsive form of epilepsy which is initiated by a generalized, bilateral paroxysmal discharge of the cerebral cortex. The ictal event is characterized by an abrupt interruption of consciousness with a typical duration of less than twenty seconds. During this time, the epileptic stops all ongoing motor activity and appears to stare. For the duration of the seizure the person is unreceptive and non-responsive to all stimuli. The attack ends abruptly with amnesia for the ictal event, however, disorientation and fatigue are rarely present (Gallagher, 1977).

Complex-partial epilepsy is a localized or focal epilepsy with its origin confined to a functional and/or anatomical group of neurons usually in the temporal lobe. Seizures are initiated by a unilateral, focal, paroxysmal discharge which results in impairment of consciousness and various degrees of amnesia. Complex-partial is characterized by automatism: the most common behaviors of this syndrome are pulling at clothing, smacking the lips, patting a leg and walking in circles. A 1 to 2 minute duration is common for this type of seizure. The epileptic is often disoriented, confused and/or amnesic for the ictal event (Gallagher, 1977).

A second form of focal epilepsy is partial-elementary. Unlike complex-partial epilepsy, consciousness is maintained with no amnesia of the ictal event. Seizures are characterized by a variety of sensory experiences including: auditory experiences (buzzing or ringing noise); visual experiences (flashing lights, bright or dark spots, colors); olfactory and gustatory sensations (unpleasant smells
and taste); and tactile sensations (localized parathesia or dysesthesia). These sensory events may accompany complex-partial seizures. Seizure duration varies from seconds to hours (Gallagher, 1977).

Two or more of the three major types of seizures mentioned above can be expressed in the same person at different times. This is called mixed seizure activity. There are a number of less frequent forms of epilepsy including Jacksonian, akinetic, febrile, sensory and gastric. These epilepsies have a wide range of etiologies and a wide variety of manifestations, many of which have received little investigation to date (Gallagher, 1977). The less frequent forms of epilepsy can also form a component of mixed seizure activity.

**Medical Treatment Modalities**

All forms and manner of treatments have been used to cure epilepsy from trephining and exorcism to drugs and neurosurgery (Temkin, 1971). Over the past few decades drugs have become the predominant, if not sole, method of seizure control. With the development of the Hydantions (Dilantin) in the 1930's, and the use of phenobarbital, a large number of patients with major motor seizures reduced seizure activity. The development of other anti-convulsant drugs, such as Carbamazepine (Tegretol), Primidone (Mysoline), Sodium Valporate (Depakane), have allowed people to experience a reduction in seizure activity. Unfortunately, benefits are frequently accompanied by an increase in unpleasant and sometimes damaging side effects. Dilantin, the most widely used
anti-convulsant, has as many as 33 possible side effects; these include drowsiness, irritability, gingival hyperplasia, anorexia, blood dyscrasias, liver toxicity and degeneration of cerebellar neurons (Vida, 1977). In some cases these side effects can cause more severe problems than the seizures themselves. Today approximately 75-80% of the epileptic population has seizure control through anti-convulsants. The remaining 20-25% are refractory, either due to the ineffectiveness of the drugs, or because of the severe side effects (Sterman, 1977).

Other approaches have also been used to help reduce the seizure activity of epileptics. One of these approaches is a special nutrition plan, known as a Ketogenic diet. This diet is very high in fat and very low in protein. It has been found to be effective, for some children under the age of seven who have severe generalized or partial seizures. The Ketogenic diet has been found to be unhealthy for adults and very difficult to manage for children. The effective mechanism for the Ketogenic diet is unknown (Gercken, 1978; Temkin, 1971).

Neurosurgery of varying types is another approach that has been effective for a very limited number of epileptics. For an epileptic to be considered a candidate for neurosurgery, the etiology must be a readily accessible lesion; in addition, the seizure activity must be severe and refractory to all medical regimes. When the above criteria are met, neurosurgery can be used effectively to ablate the epileptogenic lesion and reduce seizure activity; but only when the
Ablation will not impair brain function (Temkin, 1971).

**Biofeedback Treatment**

The newest approach for the treatment of epilepsy is the use of EEG biofeedback to help the epileptic gain control over seizure activity.

This field began when Sterman and Wyrwicka (1967), in a sleep experiment, trained cats to increase the amount of 12-14 hertz (Hz) EEG activity over the sensorimotor strip. The sensorimotor strip is located on the anterior and posterior sides of the central sulcus. Because this 12-14 Hz rhythm originates from the sensorimotor strip, it is called the sensorimotor rhythm (SMR). Sterman, Lopresti, and Fairchild (1969), used the SMR trained cats, in addition to other laboratory cats, for subjects in a drug induced seizure study. A toxic chemical, monomethylhydrazine, was administered to the subjects at a 9 mg/kg dosage level. This level was pre-determined to be a 100% convulsive dosage. It was noted that many of the cats were not having seizures or the seizures were occurring after long delays. It was discovered that these cats had been in Sterman and Wyrwicka's (1967) sleep study which resulted in increased SMR activity. It was postulated that by training an epileptic to produce more SMR activity a decrease in seizure rate might occur.

Sterman and Friar (1972) followed this realization with a case study demonstration of a decrease in epileptic seizure rate with the use of EEG biofeedback. The subject, a 23 year old female with an 8 year history of medically uncontrollable, generalized tonic-clonic
epileptic seizures, was trained to increase SMR over a 3 month period with three, 30 minute sessions per week. During the training period, seizure activity showed a significant and abrupt reduction from 2 seizures per month to .5 per month. Other researchers, (e.g., Seifert & Lubar, 1975; Lubar & Bahler, 1976; Finley, 1976; Wyler, Lockard, Ward, & Finch, 1976; Kaplan, 1975) continued exploring EEG biofeedback, by trying varying methods such as, SMR enhancement, beta enhancement, and theta suppression to control seizure activity. A brief review of these methods and their results will give a clearer idea of the work that has been done in this field.

The greatest amount of research to date in biofeedback/epilepsy control has involved the sensorimotor rhythm. This rhythm is prominent and well defined in cats as 12-16 hz activity over the sensorimotor strip. However, it is not clear if this same 12-16 hz frequency band in humans is the analog to SMR in cats. The uncertainty is partly due to the very low, 5-15 microvolt (uV) amplitude of human 12-16 hz activity which makes it very difficult to detect. Because of the difficulty in detection, the exact frequency range is also uncertain. Sterman and Friar (1972) originally defined SMR as 12-14 hz over the Rolandic cortex and it is still the most common definition. However, 11-13 hz and 12-15 hz ranges have also been used for SMR training (Finley, Smith & Etherton, 1976; Sterman, 1977). Another factor in the uncertainty over SMR is that a primary behavioral characteristic of cats producing SMR activity, is a rigid, motionless posture. In humans this is not the case; instead, it was
found by Gestaut (1952) that a 7-11 hz frequency band correlated with contralateral blocking of movement in humans. This 7-11 hz rhythm, called the mu or wicket rhythm, was studied by Kuhlman (1978) and it was estimated to be present in about 50% of the normal population. Kuhlman (1978) concluded that mu was the analog to feline SMR and that it could be considered a "somatosensory alpha rhythm" that is indicative of an "idling" function. Sterman and Friar (1972) and Lubar and Bahler (1976), on the other hand, have stated that 12-14 hz SMR is a distinct rhythm from mu. While it is scientifically interesting to determine whether 12-14 hz or 7-11 hz is the equivalent to feline 12-16 hz SMR, a much more crucial point to be considered is how well training in these frequencies will reduce seizure activity in refractory human epileptics.

Sterman, Macdonald, and Stone (1974) trained four epileptics with mixed and major motor seizures in 12-14 hz reinforcement and suppression of ≤ 10 hz. Training consisted of three, 30 to 50 minute sessions per week for 6-18 months. All four subjects experienced a reduction in seizure frequency, however, two subjects experienced very significant reductions. A 6 year old male with mixed tonic-clonic and absence seizures reduced the activity from 12 to 2 major motor seizures per week. An 18 year old epileptic with mixed akinetic and tonic-clonic seizures reduced seizure rate from 56 to 21 seizures per week. The EEG in all four subjects demonstrated a gradual reduction in high voltage slow waves and spikes while SMR was rarely detected. High voltage slow waves, spikes, polyspikes and
sharp waves are considered abnormal for an adult in the wake state and indicative of the ictal and/or interictal EEG activity of most epileptics.

Seifert and Lubar (1975) and Lubar and Bahler (1976) were successful in helping to reduce the seizure activity in seven out of eight epileptics whose seizure types included absences, mixed, complex-partial and tonic-clonic. The training involved reinforcing 12-14 hz activity and suppressing 4-7 hz production in three, 40 minute sessions per week for 6 to 9 months. SMR production demonstrated little change after training and for the most part was seen only in 1 or 2 second bursts. High voltage slow wave production was consistently demonstrated to decrease with training and was associated with seizure reduction. The one grand mal epileptic, a 12 year old male, who did not experience significant seizure reduction also did decrease slow wave activity or increase SMR production. The subject that demonstrated the greatest seizure reduction also demonstrated significant decreases in slow wave activity but only infrequent bursts of SMR. This subject, a 19 year old female, decreased her complex-partial seizure rate 20 seizures per month to 0. The poorest results were from a 26 year old female whose complex-partial seizure activity remained at approximately 20 per month, however, the seizures were of shorter duration. This subject exhibited a gradual decrease in slow wave activity and seizure reduction was not performed in these studies.

In two case studies by Finley (1977), both subjects experienced
seizure reduction from reinforcement of 11-13 hz and suppression of ≤10 hz. The subjects received three, 60 minute sessions per week for the 6-9 month experiment. The first subject, a 13 year old male who was experiencing 8 atonic seizures per hour, decreased his seizure rate to 1/3 seizure per hour after training. Epileptiform discharges (slow waves, spikes, etc.) decreased from 45% to 15% of the EEG output. The second subject, a 24 year old male with complex-partial seizures, decreased the seizure rate from 10 per month to 2 per month. The subject's EEG was normal before and after treatment. SMR activity was found not to be statistically correlated to reduced seizure activity. Kaplan (1975) trained a tonic/clonic and an akinetic epileptic with 12-14 hz reinforcement in a replication of Sterman and Frair (1972). Each subject received three, 30 minute training sessions per week for 4 months. However, it was not possible to obtain an increase in SMR production, change in EEG patterns or reduction in seizure activity. A methodological factor that might account for Kaplan's results was the use of a very strict analog/digital filtering system instead of the analog filter system that Sterman used. Kaplan postulated that due to the bell-shaped response curve of analog feedback systems Sterman's analog system gave feedback over a range wider than 12-14 hz. To correct this, Kaplan used a Krohn Hite analog/PDP-12 digital system that gave binary feedback only over the 3 hz range of SMR. This system guaranteed that only 12-14 hz activity was reinforced. However, due to the on-off nature of binary feedback and the array of
feedback modes used, proper shaping and task learning was probably made difficult. Kaplan acknowledges that the filters were "strict" (Finley, Smith, & Etherton, 1976); nevertheless, the results were interpreted as indicating no distinct 12-14 Hz SMR exist in these subjects (Kaplan, 1975). These data are supported by Kuhlman (1978) in which three normal subjects failed to demonstrate 12-14 Hz increases. In addition, recent work indicates that 12-14 Hz in humans is not analogous to 12-16 Hz SMR in felines (Kaplan, 1979).

By far, the narrow range of SMR has been the most thoroughly investigated bandpass, but other frequencies in the beta range have also been tested. In one phase of Sterman's study (1977), 18-23 Hz was selected for reinforcement while 6-9 Hz was suppressed. Based on the preliminary results from a 28 year old male tonic-clonic epileptic, this training was found to be effective in reducing slow wave activity and resulted in a cessation of his seizure activity. Preliminary results from other subjects have been equally encouraging. In a study by Wyler, Lockard, Ward, and Finch (1976), five subjects with focal or complex-partial epilepsy were trained in 14-30 Hz reinforcement while suppressing ≤ 14 Hz. Four out of five subjects demonstrated a reduction in either seizure frequency or severity. It was concluded from this study that beta activity has a seizure disruptive influence that results from the non-specific enhancement of high frequencies. Sterman (1977) has also concluded that high frequency training is beneficial in controlling epilepsy.

Some research has been conducted in low frequency ranges to
determine if theta and alpha can be effective for epilepsy control. Kaplan (1975) trained three subjects with either absence, akinetic or complex-partial epilepsy in 6-12, (theta-alpha) production. Two of these subjects, (absence, complex-partial) showed decreases in seizure activity, even though increases in 6-12 hz activity and decreases in slow wave activity were not demonstrated based on power spectral analysis (Kaplan, 1975). Due to the lack of demonstrated EEG changes, Kaplan explained these results by suggesting that the subjects had learned to increase relaxation which resulted in a lowered level of arousal and therefore decreased seizure activity. There is currently some doubt that relaxation could account for reduced seizure activity, as supported by the following experiment.

Wyler, Lockard, Ward, and Finch (1976), trained a 21 year old complex-partial patient for increased relaxation by using scalp EMG feedback. After twelve 50 minute sessions of EMG training, the seizure rate was unaffected. Kuhlman and Allison (1977) stated that with EEG training the first signs of decreased seizure activity appear after approximately 4-6 sessions. The limited information available indicates that increased relaxation can not account for reduced seizure activity.

Sterman (1977) trained five subjects with varying types of epilepsy for the production of 6-9 hz activity (theta/alpha). After a 3 month training phase the EEG patterns and the seizure rates were clearly unimproved and in some cases they were exacerbated. One subject, a 19 year old female with a 6 year history of tonic-clonic
seizures received 6, 30 minute sessions per week of 6-9 hz reinforcement for 3 months. After training, the EEG continued to show the same abnormal high voltage epileptiform activity. In addition, the seizure rate remained constant at 1.0 to 1.1 seizures per month. Following 3 months of 12-15 hz training the overall EEG voltage and epileptiform discharge rate decreased significantly. Seizure rate after 12-15 hz training dropped from 1 to 0 seizures per month. When 6-9 hz training was reinstated, the EEG gradually returned to its previous abnormal condition. Seizure rate also increased to .9 per month. Based on this evidence, Sterman found no indication of seizure reduction from rewarding these lower frequencies either due to EEG training or possible increased relaxation. Gerckens (1978) trained five complex-partial patients for simultaneous 9-13 hz (alpha) reinforcement and 1-8 hz (delta/theta) suppression. After 10 weeks of 3 to 4, 90 minute training sessions per week, four of the five subjects experienced significant seizure reduction. The EEG for four subjects demonstrated augmentation of mid-frequencies, however, slow wave activity was not simultaneously decreased. Noting the above results from Kaplan (1975), Gerckens (1978), and Sterman (1977) it could be postulated that frequencies below 9 hz are ineffective or even contraindicated for seizure reduction, while frequencies over 9 hz are potentially beneficial for seizure reduction. In fact, Sterman (1977) concluded that "EEG feedback training, involving central cortical frequencies ranging between 9-20 hz, can produce
quantitative reductions in both EEG and clinical manifestations of epilepsy" (p. 193).

Rationales for EEG Biofeedback Effectiveness

What are some of the possible explanations for the beneficial results of EEG training? In addition to the relaxation hypothesis, Kaplan (1975) has suggested that the EEG biofeedback training helps normalize the EEG patterns of the epileptic. It is well known that, in general, when compared to a normal EEG epileptics have an EEG pattern of very little mid-frequency activity and too much low frequency and/or occasionally high frequency activity (Lubar, 1980[b]). This distribution of the EEG is considered abnormal. Kaplan's conclusion (1975) was that by training in mid-frequencies while suppressing theta there are decreases in the slow wave activity and increases in mid-frequency activity. These changes constitute a redistribution of the EEG pattern. This is termed normalization. Therefore any changes in the EEG that reduce abnormal components (i.e., delta/theta activity, excessive beta activity, high amplitude levels) can be considered a form of normalization. The components of normalization would vary from subject to subject depending on the types of abnormal components involved.

Even though Gercken's research, (1978) shed doubt on the process of simultaneous augmentation of mid-frequencies and suppression of low frequencies, it was found that of the four complex-partial subjects who experienced a seizure reduction, 3 produced a significant decrease in 1 to 6 hz activity, but no change in 6 to 9
hz activity. The findings lend support to Kaplan's normalization hypothesis (1975).

Seifert and Lubar (1975) have stated that increasing evidence suggests that 12-14 hz SMR exists in humans and is distinct from either alpha or mu. They base these conclusions partly on Finley's (1976) study which demonstrated an SMR acquisition curve and increased seizure activity during non-contingent feedback. Noting that 16 out of 17 patients have experienced seizure reduction from SMR training, SMR's seizure control properties appear clear (Sterman, 1977). However, it should be noted that additional researchers (e.g. Gercken, 1978; Sterman and Macdonald, 1978; Wyler, Lockard, Ward, & Finch, 1976; Kuhlman & Allison, 1977) have found 9-13 hz, 18-23 hz, 14-30 hz and 9-14 hz ranges to be effective in reducing seizure activity with a wide range of epilepsies. While SMR is effective for seizure reduction, the above evidence indicates that other frequencies have this property as well.

Wyler, Lockard, Ward, and Finch (1976) have proposed a desynchronous EEG activity hypothesis based on research with monkeys and humans. It was found that with two human subjects with frontal focal epilepsy, synchronous EEG activity (high voltage, slow waves) increased seizure rate and desynchronous EEG activity (low voltage, fast waves) decreased seizure rate. Wyler, Lockard, Ward and Finch (1976) concluded that any frequency, as long as it is known not to initiate seizure, would be of benefit if it desynchronized the EEG. However, they warn that without further research these findings can
not be generalized to other types of epilepsy.

Gerckens (1978) discusses the mechanism of biofeedback/epilepsy control in terms of hypersynchrony and synchronous single unit activity. Synchronous single unit activity refers to the synchronous firing of cortical neurons. This is distinct from synchronous EEG activity which refers to regular, repeating EEG waves that are characteristic of alpha and theta. Hypersynchrony is characterized by excessive synchronization of single unit discharge activity and an increase of discharge rates from these individual cells. Hypersynchrony is considered the keystone of seizure production. Based on a postulate by Andersen and Andersson (1968) the thalamus underlies the generation of synchronous rhythms, primarily slow wave and alpha rhythms with both excitatory and inhibitory functions being associated with this synchronous activity. It is the inhibitory synchronous activity that inhibits the recruitment of adjacent neural areas thereby preventing hypersynchrony.

The role of the thalamus is further clarified by Andersen and Andersson (1968) when it is stated that distributor interneurons of the thalamus when activated by a frequency that is close to the inherent thalamic rhythm would impose this rhythm upon a large number of cortical cells and thus cause synchronization. Frequencies that produce the greatest amount of synchronization deliver their stimuli to the thalamic nuclei at the end of the post inhibitory rebound of the cell thus causing a phased summation effect and increased synchronization. Activation by a frequency higher than the thalamic
rhythm would not impose rhythmic spread because the stimulus arrives out of phase with the post inhibitory rebound and thus eliminates the summation effect which now leads to desynchronization. Whether or not this is the actual mechanism is far from clear, primarily because of our limited knowledge of the brain's functional mechanisms. However, the above hypothetical explanation coincides with the empirical conclusions that desynchronous activity leads to decreased seizure rates (Wyler, Lockard, Ward, & Finch, 1976) and that the more desynchronous activity (9-20 Hz) should also reduce seizure occurrence (Sterman, 1977).

Placebo effect was initially offered as an explanation for seizure reduction with EEG training. Placebo effect can be defined as a positive therapeutic response to a neutral treatment. It is well known that the placebo effect has its greatest influence in the very beginning of a treatment and this influence declines over time. With EEG biofeedback training it was noted that seizure reduction started later and improved over time (Sterman, 1977). Gercken (1978), Wyler, Lockard, Ward, and Finch (1976), and Finley (1977) used a non-contingent phase which has clearly demonstrated that seizure reduction is negatively affected when non-contingent feedback is used. This evidence indicates that placebo effect plays a very small part in seizure reduction through EEG training (Kuhlman and Allison, 1977).

Another possible explanation might be that it is not the specific frequency but rather the amplitude that is important in
reducing seizure rates. Sterman, Macdonald, and Stone (1974), Seifert and Lubar (1975), Lubar and Bahler (1976) and Sterman (1977) have all noted a consistent decrease in slow wave activity with SMR training for most subjects who experienced seizure reductions. As was stated previously, often the subject who experienced the greatest seizure reduction also demonstrated the greatest decrease in slow wave activity. It is well known that frequency and amplitude have an inverse relationship, such that low frequencies have a high amplitude and high frequencies have a low amplitude (Sterman and Macdonald, 1978). Therefore, by training an epileptic to increase the percentage of high frequencies or decrease the low frequencies, the amplitude or the voltage of the EEG is indirectly decreased. It can be hypothesized that the decrease in amplitude could account for the decreased seizure rate. To date, little research has been initiated to investigate the role amplitude plays in seizure control. In the Lubar and Bahler (1976), Finley (1977), and Sterman, Macdonald, and Stone (1974) studies, inhibitory circuitry was used to assure that only 12-14 hz activity was reinforced. This inhibitory function eliminated the possibility of studying the effects of amplitude (Lubar & Bahler, 1976).

One of the few studies that has looked at the power variable was Finley (1977). A complex-partial subject was trained over a 6 month period with 12-14 hz reinforcement and 4-7 hz suppression. It was found that for 12 hz the overall voltage had increased by .42 uV, but during the same time period theta, which had been suppressed,
significantly increased voltage by 1.1 uV. During this time period, the seizure rate for this patient dropped significantly from approximately ten seizures a month to two. Overall it was found that as the voltage of SMR increased the voltage of theta also increased. However, as the voltage of SMR and theta increased the power of the raw EEG decreased. Even though these results are based on one client and may be idiosyncratic, it lends some light to the possibility that it is not the specific frequency band but rather a change in the voltage that is important.

In most studies, amplitude has not been clearly specified as an experimental variable, even though two SMR studies have set a lower limit of 5 to 7 uV, for 12-14 hz while the upper cut off was seldom mentioned (Sterman and Macdonald, 1978; Lubar & Bahler, 1976). This probably is because with SMR wave patterns a 20 uV wave could be considered vary large; however, with alpha, amplitude becomes much larger and must be taken into account. It is well known that high voltage waves are a hallmark of epilepsy, but when training for EEG enhancement, exactly how much amplitude must be present before it is considered epileptogenic is not clearly defined. Sterman and Macdonald (1978) set an overall limit of 50 uV so that any activity over 50 uV would be considered epileptogenic and not reinforced. In Gercken's (1978) experiment 100 UV was set as the upper limit so that activity over this level was said to be epileptogenic. The difference between these two levels is primarily due to the need for a higher cut off level for the alpha amplitude range. For most
mid-frequency training, a cut off of 100 uV would seem to be the more practical.

From the review of the literature, it is clear that biofeedback/seizure control is not solely restricted to a specific narrow range of frequencies for significant seizure reduction. In addition, both Wyler, Lockard, Ward, and Finch (1976) and Sterman and Macdonald (1978) have stated that desynchronous, low amplitude, fast waves are more effective for seizure control than synchronous high amplitude, slow waves. Also from reviewing the literature it was noted that a number of studies reported a consistent decrease in slow wave activity that was frequently associated with decreased seizure activity. It was hypothesized that the decrease in slow wave activity corresponded with a decrease in amplitude of the EEG. This decrease in amplitude was hypothesized to be responsible for the decrease in seizure activity. In light of the fact that amplitude is a common variable and that very little research has been published on the specific role of amplitude, it seems a logical step to look at the relationship between amplitude and seizure reduction. A significant question to ask in relation to amplitude is whether training a subject to produce high amplitude mid-frequencies would produce the same results as training a subject to produce low amplitude mid-frequencies. The hypothesis to be tested states that the seizure rate decreases and is significantly lower for subjects trained in low amplitude (10-25 uV) mid-frequency (9-13 Hz) augmentation than those trained for high amplitude (60-75 uV).
mid-frequency (9-13 hz) augmentation. The purpose of this experiment is to provide data for the evaluation of this question and help broaden the understanding of biofeedback's function in the control of epilepsy.
Subjects were selected on three main criteria: seizure history, frequency of seizures, and ineffectiveness of anticonvulsant medications. Each subject had a clear history of uncontrolled generalized, partial or mixed seizure activity for approximately 5 years prior to the study. Subjects were limited to persons between the ages of 10 and 65. These subjects were referred by the Epilepsy Association of Central Florida and local neurologists. Medical screening for subjects was accomplished via evaluation of history, neurological examination and EEG records. These were performed with the aid of a neurologist and the Epilepsy Association of Central Florida. Each subject had given full compliance to previous regimes of anticonvulsant therapy with resultant inadequate control. Each subject had approximately five seizures per month, with verification by medical personnel, family members or friends. A total of 4 subjects participated in, and completed, the 15 week experiment. The original pool of subjects consisted of 25 epileptics. Due to medication non-compliance, low motivation, severe psychological and personality problems, poor seizure verification, and the large amount of time required for the study, all but four of the subjects were eliminated. Of the four subjects, two were randomly assigned to high amplitude training and two to low amplitude training.
Subject profile: S1

S1 is a 34 year old married caucasian male of average intelligence with a 25 year history of complex-partial seizure activity. A right temporal lesion of unknown etiology precipitated seizure onset at the age of nine. Seizure activity is reported as starting with an aura characterized by pain over the left eye followed by bright spots or "stars" in the visual field. The aura duration is approximately 15 seconds, with seizure activity lasting for 1 to 2 minutes. The seizure is composed of loss of consciousness, aimless walking, drooling, and automatisms such as smacking lips, mumbling and pulling at clothing. After a seizure, S1 is usually disoriented and sleepy for a short period of time. S1's daily medications included: Dilantin, 500 mg; Depakane, 1000 mg; and Mysoline, 1000 mg. Gas Liquid Chromatography (GLC) results indicated that all drugs were within the therapeutic range and remained relatively stable for the duration of the experiment.

Subject profile: S2

S2 is a 21 year old single Hispanic female of above average intelligence with a seizure history of 12 years starting with tonic/clonic seizures at the age of nine. Seizure control was obtained with phenobarbital; however, during her teens complex-partial seizure activity began. A right temporal focus was found and all following EEG's were consistent with this finding. S2's complex-partial seizure activity is characterized by a feeling of anxiety or fear, then loss of consciousness. These are followed
by some clonic movement of arms and hands, spitting, and automatisms such as saying the same word repeatedly, pulling at clothing or a patting motion of the hands. Postictally, there is a short period of disorientation as well as amnesia and head pain. Seizure duration is usually of 1 to 2 minutes. S2 also reports having a large number of "auras" that encompass a wide variety of sensory experiences, including: olfactory (smell of burning electrical wires or bacon, hot chocolate); tactile (sensation of bugs crawling or a burning sensation on the face); or auditory (a ringing noise or bell chimes). "Auras" are only rarely associated with complex-partial seizure activity and have been reported to number over 100 per day. S2's daily medications include: Dilantin, 300 mg; Phenobarbital, 2-1/2 grs; and Tegretol, 1200 mg. GLC results indicated that all drugs were therapeutic and relatively stable for the duration of the experiment.

**Subject profile: S3**

S3 is a 27 year old single Caucasian male of below average intelligence with an 11 year history of right focus complex-partial epilepsy. Seizure onset was at age 16, with medical control being successful until age 21. At that time, complex-partial seizure activity began and was soon followed by the discovery of a right temporal subdural hematoma which was surgically removed. S3's seizure characteristics are varied; however, seizures are commonly of sudden onset with no aura. Seizures are frequently characterized by the head turning to the left, tonic extension of arms and legs, occasionally associated with movement of the legs and with arms
shaking or curling inward. Eyes remain open but non-responsive; there is some drooling and occasional urinary incontinence. Seizure duration varies from 10 seconds to several minutes, with postictal confusion and disorientation lasting for 5 to 10 minutes. S3 had been placed on numerous anticonvulsant medications, but the results have been poor. S3's daily medications included: Dilantin, 400 mg; Mysoline, 250 mg; and Depakane, 1250 mg. GLC results indicated that S3's Dilantin levels remained within the therapeutic zone, however Depakane and Mysoline were consistently below therapeutic range throughout the experiment.

Subject profile: S4

S4 is a 55 year old married Caucasian female of above average intelligence with a history of partial-elementary, complex-partial, tonic/clonic, and absence seizures. Absence seizure activity commenced after an automobile accident 19 years ago. Another serious automobile accident produced lesions on the frontal lobe as well as the left and right temporal lobes approximately 3 years prior to the experiment. This appeared to be the antecedent to partial seizure activity including elementary, complex and generalized types. Partial-elementary seizures were characterized by olfactory sensations (smell of burning electrical wires, bacon, sugar), tactile sensations (something touching the skin, numbness around the mouth), visual experiences (light explosions), or auditory events (buzzing noise).

S4's complex-partial seizure activity usually started after a
series of warning symptoms which included the development of a severe pain on the left temple which migrated over the head to the right temple then spread to the right forehead and behind the right ear. A buzzing noise in the left ear, as well as the olfactory and tactile sensations described above occasionally accompanied the pain. Seizure activity began when the pain became very intense behind the right ear and consciousness was lost. Complex-partial seizure activity was characterized by automatisms such as a patting motion of the hands, walking aimlessly, lip smacking and clawing at clothing. On occasion, seizures generalized to a lateral or bilateral tonic/clonic seizure. Nocturnal generalized partial seizures were noted to occur sometimes during the early morning hours and were always associated with urinary incontinence. Seizure duration varied depending on the type of seizures involved. Partial-elementary seizures, for which there was no loss of consciousness lasted from seconds to hours. Complex-partial and generalized seizures usually lasted 2 to 4 minutes with amnesia, nausea and postictal confusion lasting 5 to 10 minutes.

S4's daily medication included: Dilantin, 400 mg and Phenobarbital, 2 gr. GLC results indicated that Dilantin levels became toxic during the first month of training therefore, Dilantin dosage was decreased to 300 mg per day. Phenobarbital levels remained stable and therapeutic for the duration of the experiment.

Prior to the initiation of this experiment S4 began to develop periodic symptoms of vertigo characterized by dizziness, nausea, and
headaches. The final diagnosis was viral infection of the right labrynthene system. S4 expressed a deep desire to participate in the experiment despite the vertigo and was allowed to do so. Vertigo symptomatology continued at varying degrees for the first 3 months of training. Also during this period S4 was afflicted with several additional viral infections that produced severe flu-like symptomatology. All symptomatology reached peak severity during the second month of training. By the fourth month of training vertigo had greatly diminished and all other viral symptomatology had abated.

**Apparatus**

The primary component used in this study was the Autogen 120A EEG Wave Form Analyzer. This unit has variable bandpass filters for a 2-20 hz range, and an amplitude range of 10-150 μV. The 120A was used to measure frequency, amplitude and percent time in the main bandpass, (9-13 hz) and percent time in the auxiliary bandpass (2-8 hz). The main bandpass was used to provide analog auditory feedback. A sound (theta alarm) was emitted when the frequency output fell 1 hz or more below the lowest frequency of the main bandpass (≤8 hz). The auxiliary mode did not provide feedback but did record percent time of 2-8 hz.

The Autogen 120A uses a zero-crossing analysis system to analyze EEG wave forms. With this system, the subject must produce six successive zero-crossings in the specified criterion range to receive feedback.

The Autogen's combined digital/analog analysis system provides
precise discrimination of dominant EEG frequencies while providing analog feedback over this precise range. The digital/analog system prevents high amplitude waves that are outside the chosen frequency range from passing through the system and "ringing" the filters. This feature eliminates erroneous feedback.

The Autogen 5600 with the attached alpha-numeric printer was used to tabulate the data from the 120A and produce a paper printout of this information. Means of frequency, amplitude and percent time of both 9-13 hz and 2-8 hz were provided.

The Autogen 1700 EMG unit was used to obtain pre- and post-muscle tension baselines. A standard shielded EMG electrode with contact medium, was used. Adhesion to the frontalis muscle was accomplished with electrode attachment adhesive discs.

Procedure

The subjects who met the selection criteria and were available to participate in this study were given a pre- and post-evaluation. Pre-evaluation included EEG, neurological, abbreviated Minnesota Multiphasic Personality Inventory (Mini-Multi) and Mostovsky seizure questionnaire. The post-evaluation included reassessment by all procedures but the EEG.

Each subject received a copy of the article "An introduction to Biofeedback", (Fuller & Sempell, 1977) during the first session. In addition, the nature and implications of biofeedback, as well as the nature and procedure of this experiment, were discussed. The possibility of this experiment facilitating a seizure or increasing
the over-all seizure rate was discussed with each subject. It was explained that EEG training has been demonstrated to have varying degrees of effect on subjects and that the greatest risk was the possibility of a temporary increase in seizure activity during the experiment. Also, personnel on hand at the laboratory were trained to handle any seizure activity that might occur.

Subjects maintained their anticonvulsant medications at a relatively constant level through the entire study, as prescribed by their neurologist. Their compliance was determined by bi-weekly gas liquid chromatography (GLC) tests, which measures anticonvulsant medication blood levels. Subjects were given a seizure diary approximately 2 months prior to the experiment's initiation. The seizure diary was maintained for a 2 month baseline, during the experiment, and then a 2 month follow-up. The subjects indicated by day and time the occurrence of seizures and when possible, a subjective, qualitative rating of intensity, duration and nature. Family members and friends were asked to closely observe the subject and monitor the diary to assure accuracy. Subjects were required to present their diaries for review twice a month during the baseline period and once a month during the treatment to assure their compliance and understanding.

Each subject attended 3 to 4 sessions a week for one and a half hours, with 40 minutes of this time being used for electrode placement, removal, and discussion. The remaining 50 minutes were used for the actual trial. EEG biofeedback electrode placement was
on the right hemisphere (T4-C4) using the 10-20 International system. The referents are located over the sensorimotor strip of the right hemisphere.

The subjects were seated in a comfortable reclining chair in a small room. The experimenter and equipment were behind the subject, with the data analyzer and digital printer in a separate room. A speaker was used to provide auditory feedback to the subject when appropriate criteria were met. The subject was instructed to maintain eyes in a closed position except for the 60 second rest period when data were not collected. A diagram was available in the room to help the subject visualize the task. (see appendix A)

There were two types of training: 1) high amplitude training; and 2) low amplitude training. In both types, the feedback frequency range remained constant at 9-13 Hz; i.e., when the EEG output dropped below 9 Hz an alarm sounded, and when the output was above 13 Hz, feedback terminated. With the output in the 9-13 Hz range the subject received analog tone feedback. The feedback consisted of an analog auditory tone that varied in volume, thus indicating amplitude change within the bandpass (high volume-high amplitude, low volume-low amplitude) and pitch indicating frequency changes within the bandpass (high pitch-high frequency, low pitch-low frequency). Feedback commenced when the subject produced six successive zero-crossings in the 9-13 Hz or the 2-8 Hz range. Subjects receiving high amplitude training were shaped to meet a criterion range between 60-75 µV in the 9-13 Hz bandpass. Lower and upper
amplitude cutoffs were initially set at 10 and 75 uV, respectively. Feedback was not given for waves above 75 uV to prevent the reinforcement of epileptogenic activity. When the average percent time reached 80% for five minute segments of 9-13 Hz activity, the lower amplitude cutoff was raised by 5 uV's. To assure stability at the changed amplitude, the following was required: If the percent time at the new amplitude level was 60 or greater, the subject continued at the new level until 80 percent time was achieved. The process then repeated. If percent time dropped below 60, the lower amplitude cutoff was decreased to its previous level or a level that produced a percent time of 60 or greater. The shaping process continued until the amplitude criterion was met or 45 sessions had been completed.

Subjects receiving low amplitude training were shaped to meet a criterion between 10 and 25 uV. Lower and upper amplitude cutoffs were initially set at 10 and 75 uV, respectively. When the average percent time reached 80% for each 5 minute segment, the upper amplitude cutoff was decreased by 5 uV's. As previously, if the percent time at the new amplitude level was 60 or greater the subject remained at that level until 80 percent time was achieved. The process then repeated. If the percent time dropped below 60, the upper cutoff was returned to the previous level or a level that produced a percent time of 60 or greater. The shaping process continued until the amplitude criterion was met or 45 sessions had been completed.
Pre and post EMG level determinations were performed. Muscle tension levels were measured concurrently with EEG feedback during the 50 minute trials of sessions 6 and 35. The Autogen 1700 with shielded EMG electrodes was used for this purpose. Electrode placement was on the frontalis.

**Experimental Design**

Each subject completed 45, 50 minute trials. Each trial of each session was divided into 10, 5 minute segments. The amplitude (10-25 uV, 60-75 uV) and frequency (9-13 hz) criteria were set during segments 1 and 10 (that is, the initial and the final 5 minute periods). Shaping varied the amplitude settings during segments 2-9. For this reason data for comparison were taken only from segments 1 and 10 of each trial. To encourage generalization, subjects were instructed during segments 1 and 10 to continue performing without feedback, as they had while producing large amounts of feedback. The Autogen Data Acquisition Center allowed a 60 second rest period between each 5 minute segment when data were collected. This minute was used to inform the subject of the percent time in alpha and theta, and, in general to encourage the subject to produce the analog tone and keep the theta alarm off.

The first five sessions were used as baseline, therefore no feedback was given during this time. Half of each baseline session was used for a general open frequency, open open amplitude baseline. The other half of each of the 5 baseline sessions was used to obtain data within the frequency and amplitude criteria for the two types of
training. Sessions 6 through 45 were used for contingent feedback based on the amplitude criterion.
III RESULTS

Due to the small N as well as the high degree of variability both within and between subjects, statistical analyses were considered inappropriate. For this reason, each subject will be viewed as a case study. Data will be presented for each subject on the following parameters: seizure rate, amplitude, frequency, percent time of 9-13 hz at criterion amplitude and percent time of 2-8 hz.

Data for each session were based on data recorded from segments 1 and 10. During these segments the frequency and amplitude criteria were measured. Data used for comparison were the average of five consecutive sessions starting from baseline. This produced nine points of data, representing the averaged activity over the past five sessions. Each five session block roughly corresponded to a two week period. Seizure activity was measured for each two week period and used for comparison with the concurrent EEG parameters.

Subject Results: S1

Seizure activity (see Figure 1)

S1 had recorded baseline seizure rates averaging 5 complex-partial seizures per month. During training blocks 1 and 2 (sessions 6-15) average seizure rate increased slightly to six then remained stable for blocks 3 and 4 (sessions 16-25). Seizure rate decreased during training blocks 5 and 6 (sessions 26-35). Seizure
activity declined sharply to two seizures per month in the final phases of training (blocks 7 and 8, sessions 36-45). Seizure rate remained at 2 seizures per month for the first month of follow-up. For the second month of follow-up, seizure rate increased to four. The average seizure rate of the final month of training and the two months of follow-up indicated a seizure reduction of 2.7 seizures per month from baseline.

Amplitude (see Figure 2)

S1 rarely reached or maintained the criteria of 9-13 Hz at 60-75 uV. Amplitude averaged over the five consecutive sessions of baseline was 36.4 uV. During blocks 1 through 4 (sessions 6-25) average amplitude dropped to 30.5-33.1 uV. During blocks 6-8 (sessions 31-45) average amplitude started at its highest point (39.9 uV) and dropped sharply to a low of 30.1 uV.

Frequency (see Figure 3)

Dominant frequency averaged over five sessions of baseline was 9.5 Hz. Average dominant frequency fluctuated less than .75 Hz over the entire experiment. Frequency increased and remained stable at approximately 10 Hz during blocks 2 through 5 (sessions 11-30). Frequency decreased to near baseline during blocks 6 and 7 (sessions 31-50). During the 8th block frequency increased again to near 10 Hz.

Percent time of 9-13 Hz at 60-75 uV (see Figure 4)

Percent time of 9-13 Hz at the 60-75 uV criterion was 1.5% during baseline. By the sixth block (sessions 31-35) percent time
had increased to 2.9%, however, it quickly dropped over the last 10 sessions to a below baseline level of .8%. Overall, there was little change in percent time 9-13 hz at 60-75 uV.

**Percent time of 2-8 hz** (see Figure 5)

Percent time of 2-8 hz had an average baseline of 27.7%. The percentage dropped to 14.1% over the first block (sessions 6-10) then fluctuated during blocks 3 and 4 (sessions 16-25). Percent time of 2-8 hz increased to 28.2% during the 6th block (sessions 31-35) then peaked at 29.4% during the 7th block (sessions 36-40). A sharp drop to 14.5% occurred in the 8th block (sessions 41-45). In general, percent time of 2-8 hz decreased over the duration of the experiment.

**Results summary: S1**

During blocks 1 through 4 (sessions 6-25) seizure activity averaged six per month. EEG parameters during this time indicated a rise in frequency and a sharp decrease in both percent time of 2-8 hz and amplitude. Seizure rate decreased to five per month during blocks 5 and 6 (sessions 26-35) and was associated with a marked increase in percent time of 2-8 hz. A sharp decrease in amplitude, percent time of both 2-8 and 9-13 hz and an increase in frequency were associated with a marked decrease in seizure rate (2 per month) during blocks 7 and 8.

For S1 percent time of 2-8 hz appeared to vary negatively with seizure rate. Other parameters did not vary consistently with seizure activity. However, the overall reduction in both percent time of 2-8 hz and amplitude corresponded to the gradual decline in
seizure rate.

Subject Results: S2

Seizure activity (see Figure 6)

S2's 2 month seizure baseline determined a seizure rate of 3.5 complex-partial seizures per month. Subjective reports of "aura" activity indicated a rate of between 80 and 100 per day. However, no verification could be performed due to the subjective nature of the experiences. Seizure activity peaked at 5 seizures per month during block two (sessions 11-15). Seizure rate decreased then remained stable during blocks 3 and 4 (sessions 16-25). Block 5 (sessions 26-30) demonstrated a drop in seizure rate to zero. Seizure activity increased to 5 per month during blocks 7 and 8 (sessions 36-45). Overall, seizure activity during training showed a slight increase to 4.5 seizures per month. This is a one seizure per month increase.

Amplitude (see Figure 7)

S2 infrequently produced criterion amplitude levels. The average baseline amplitude was 25.5 uV which was well below the 60-75 uV criteria. S2 did not increase average amplitude, rather it was reduced over the first fifteen sessions to a low of 21 uV. S2's average amplitude slowly increased over the next 20 sessions to peak at 25.9 uV.

Frequency (see Figure 8)

Average dominate frequency was recorded during baseline at 9.3 hz and fluctuated within a .5 hz range. A slight increase in frequency occurred during blocks 3, 4 and 5 (sessions 16-30). Over
the duration of the experiment, average frequency gradually declined to 8.8 Hz. Instantaneous frequency readings indicated a high incidence of theta wave activity.

**Percent time of 9-13 Hz at 60-75 μV (see Figure 9)**

The percentage of 60-75 μV, 9-13 Hz activity averaged over five sessions of baseline was .5%. This percentage declined to zero over the next sessions. Percent time of 9-13 Hz increased to its highest level (.7%) during block 7 (sessions 36-40). A decline during the final five sessions was noted, reaching .1%.

**Percent time of 2-8 Hz (see Figure 10)**

S2 had an average percent time during baseline of 40.1% at 2-8 Hz. S2's only prolonged period of decreased 2-8 Hz activity (30%) occurred during blocks 3, 4, and 5 (sessions 16-30). Extensive therapeutic interaction took place during that time to help the subject overcome a fear of success. When therapeutic intervention was terminated, average percent time of 2-8 Hz dramatically increased to its highest level (41%).

**Results summary: S2**

During block 2 (sessions 11-15) an increase in amplitude, percent time of 2-8 Hz, and a drop in frequency corresponded to the increase in seizure activity to 5 per month. Seizure rate decreased to 4 per month during blocks 3 and 4 (sessions 16-25) and was associated with a decrease in percent time of 2-8 Hz to its lowest level (29.9%). Percent time of 2-8 Hz continued at a low level while seizure rate dropped to zero during block 5 (sessions 26-30). A
sharp rise in percent time of 2-8 hz and a decrease in frequency during block 6 (sessions 31-35) was associated with an increase in seizure activity. During the final month of training (blocks 7 and 8, sessions 36-45) percent time of 2-8 hz fluctuated while seizure activity increased.

For S2, amplitude and percent time of 9-13 hz at 60-75 uV demonstrated very little relationship with seizure activity. Graphical comparison suggests an inverse relationship between frequency and seizure rate, while percent time of 2-8 hz varied positively with seizure rate.

Subject Results: S3

Seizure activity (see Figure 11)

A two month seizure baseline demonstrated an average rate of 15 complex-partial seizures per month. The first month of training (blocks 1 and 2, sessions 6-15) resulted in a marked decrease in seizure activity from 15 to 5 per month. For blocks 3 and 4 (sessions 16-25) seizure activity remained low at 6 per month with all seizures occurring on 2 consecutive days. During blocks 3 through 6 (sessions 16-35), S3 experienced the longest seizure free period (56 days) of the entire seizure history. Seizure activity started again at the very end of the sixth block (sessions 31-35) with three seizures. One seizure occurred during the 8th block (sessions 41-45). The average seizure activity of the last two months of training and the first month of follow-up indicated a seizure reduction of 12.3 seizures per month from baseline. The
seizure diary was inadequately maintained during the second month of follow-up. The limited data available indicated that seizure activity returned to baseline level during the second month of follow-up.

Amplitude (see Figure 12)

S3's average baseline amplitude was 30.7 uV. Average amplitude declined to its lowest level (25.7 uV) within ten sessions (blocks 1 and 2) and remained relatively stable for the next ten sessions (blocks 3 and 4). Average amplitude increased to its highest level (32.3 uV) during the 6th block (sessions 31-35). Amplitude declined to below baseline levels over the last ten sessions (blocks 7 and 8).

Frequency (see Figure 13)

S3's average dominate frequency was 8.1 hz during baseline which indicates that a majority of S3's EEG activity was below the 9-13 hz feedback zone. Frequency demonstrated a gradual increase over the duration of the experiment. By termination, average frequency was 9.2 hz. The only marked decline occurred during block 6 (sessions 31-35) when frequency dropped to 8.5 hz.

Percent time of 9-13 hz at 10-25 uV (see Figure 14)

S3's baseline average percentage of 9-13 hz at 10 to 25 uV was 9.3%. Percent time 9-13 hz increased dramatically over the first five sessions to 19.8% and remained above the baseline percentage throughout the experiment. The highest average percentage of criterion 9-13 hz was 23.1% during block 5 (sessions 26-30). S3's lowest 9-13 hz percentage (14.4%) occurred during block 6 (sessions
Percent time of 2-8 Hz (see Figure 15)

The average baseline percent time for 2-8 Hz was extremely high for S3, averaging 59.4%. This percentage dropped to 34.2% in five sessions and continued to decline to 17.8% during the 8th block (sessions 41-45). This demonstrates a decrease of average 2-8 Hz activity of 41.6%. The only marked increase occurred during sessions 31 through 35 (block 6) when it reached a level of 42.8%.

Results summary: S3

During blocks 1 and 2 (sessions 6-15) the seizure rate decreased to five per month and was associated with decreases in amplitude and percent time of 2-8 Hz, as well as increases in frequency and percent time of 9-13 Hz. Seizure activity remained low until the end of the sixth block, this was associated with a drop in average frequency and percent time of 9-13 Hz in addition to a sharp increase in averaged amplitude and percent time of 2-8 Hz. Amplitude, percent time of 2-8 and seizure rate decreased while percent time of 9-13 Hz and frequency increased during the 7th block (sessions 36-40).

S3's marked seizure reduction appeared to vary closely with two parameters. Amplitude varied positively with changes in seizure activity. A negative relationship appeared to exist between frequency and seizure rate. The overall reduction in percent time of 2-8 Hz and the increase in percent time of 9-13 Hz corresponded to the overall seizure reduction.
**Subject Results: S4**

**Seizure activity** (see Figure 16)

S4's average seizure baseline was recorded prior to the development of vertigo and other viral infections. The average baseline seizure rate including all types of seizure activity was 25 per month. Complex-partial and generalized seizure activity comprised approximately four-fifths of this total activity (solid line on graph). Partial-elementary seizures composed approximately one-fifth of the total (broken line on graph). Seizure rate during blocks 1 and 2 (sessions 6-15) rose sharply to more than double the baseline rate. Partial-elementary seizures accounted for the majority of the increase by rising from a baseline of five seizures per month to 17 in the first block and 21 in the second block (sessions 6-15). Complex-partial/generalized seizure activity increased by 7 per month during the first and second blocks.

During blocks 3 and 4 (sessions 16-25) partial-elementary seizure activity reached a peak of 102 seizures per month as compared to a baseline of 5 per month. Complex-partial/generalized seizure rate decreased by six seizures.

Partial-elementary seizure activity decreased from 53 in block 4 to 36 in block 5 (sessions 21-30) while complex-partial/generalized activity peaked at 20 seizures in block 5. Block six (sessions 31-35) demonstrated a continued decrease in both partial-elementary and complex-partial/generalized seizure activity.

The fourth month of training (blocks 7 and 8, sessions 36-45)
demonstrated a continued decrease in partial-elementary seizure and a sharp decline in complex-partial/generalized seizure activity.

Seizure activity in the first month of follow-up showed a continued decrease in activity. Complex-partial/generalized activity was 15 seizures per month below baseline while partial-elementary activity was about one seizure below baseline.

Partial-elementary seizure activity averaged over the last month of training (blocks 7 and 8, sessions 36-45) and the two months of follow-up demonstrated a seizure increase of 3.3 per month. Complex-partial seizure activity averaged over the same period demonstrated a 50% seizure reduction from baseline. This represents a seven seizure per month decrease.

**Amplitude (see Figure 17)**

Average amplitude never reached the amplitude criterion of 10-25 uV. Average amplitude declined to 31.3 uV during blocks 2 and 3 (sessions 11-20). Over blocks 4, 5 and 6 average amplitude increased then leveled off between 35 and 36 uV. Average amplitude decreased to its lowest levels (30.4-30.7 uV) during sessions 36 through 45 (blocks 7 and 8). Overall, average amplitude declined from a baseline of 37.9 uV to a low of 30.4 uV over the course of the experiment.

**Frequency (see Figure 18)**

S4 had an average frequency baseline of 11.5 Hz. Frequency declined to its lowest point (9.6 Hz) during blocks 5 and 6 (sessions 26-35). Average frequency increased over the final 10 sessions
Percent time of 9-13 hz at 10-25 uV (see Figure 19)

Average percent time of 9-13 hz at 10-25 uV baselined at .5%. Percent time increased to 5.6% during blocks 3 and 4 (sessions 16-25). A sharp increase occurred during block 7 (sessions 36-40) to a peak of 13%. Percent time dropped to 5.4% during sessions 41 thru 45 (blocks 7 and 8).

Percent time of 2-8 hz (see Figure 20)

The average baseline rate for percent time of 2-8 hz was 7.5% which proved to be the lowest level for the entire experiment. During the first block (sessions 6-10) percent time rose to 12.8%. By the 5th block (sessions 26-30) average percent time of 2-8 hz increased to 31.8%. During blocks 7 and 8 (sessions 36-45) percent time dropped to 13.5%. Overall, percent time of 2-8 hz remained well above baseline during the experiment, however, it dropped below baseline (5%) during a follow-up session.

Results summary: S4

While both complex-partial/generalized and partial-elementary seizures increased during block 1 and 2, EEG parameters did not demonstrate consistent change. Partial-elementary seizure activity peaked while complex-partial/generalized seizure activity decreased during blocks 3 and 4 (sessions 16-25). This was associated with a dramatic increase in average percent time of 2-8 hz with a concurrent increase and leveling in amplitude and average percent time of 9-13 hz. Frequency exhibited a marked decrease during blocks
3 and 4. Complex-partial/generalized seizure activity peaked during block 5 (sessions 26-30) while partial-elementary activity decreased. Percent time of 2-8 hz also peaked during block 5 while other parameters showed little change. A large decline in average percent of 2-8 hz and amplitude as well as an increase in frequency and average percent time of 9-13 hz during blocks 7 and 8 (sessions 36-45) corresponded to the decreases in both seizure types.

For S4, percent time of 9-13 hz varied inversely with the complex-partial/generalized seizure rate. All other parameters varied inconsistently with both types of seizure activity. In general, S4 experienced an overall increase in percent time of 9-13 hz and a reduction in amplitude, frequency and seizure rate.

Summary: Hypothesis

The hypothesis stated that the seizure rate decreases and is significantly lower for subjects trained in low amplitude (10-25 uV) mid-frequency (9-13 hz) augmentation than those trained for high amplitude (60-75 uV) mid-frequency (9-13 hz) augmentation. Of the two subjects who received low amplitude training, S3 experienced a 12.3 per month reduction and S4 experienced a 3.3 month increase in partial-elementary and a 7 per month reduction in complex-partial seizures. Of the two subjects receiving high amplitude training, S1 experienced a 2.7 per month reduction while S2 experienced a 1 per month increase. These results suggest a limited confirmation of the stated hypothesis.
Figure 1. Seizure rate of subject S1
Figure 2. Average amplitude of subject S1
Figure 3. average frequency of subject S1
Figure 4. Percent time of 9-13 Hz at 60-75 μV for subject S1
Figure 5. percent time of 2-8 Hz for subject S1
Figure 6. seizure rate of subject S2
Figure 7. Average amplitude of subject S2
Figure 8. average frequency of subject S2
Figure 9. percent time of 9-13 Hz at 60-75 uV for subject S2
Figure 10. percent time of 2-8 hz for subject S2
Figure 11. Seizure rate of subject S3
Figure 12. average amplitude of subject S3
Figure 13. Average frequency of subject S3
Figure 14. Percent time of 9-13 Hz at 10-25 uV for subject S3
Figure 15. Percent time of 2-8 Hz for subject 53
Figure 16. Seizure rate of subject S4
BLOCKS OF FIVE CONSECUTIVE SESSIONS

Figure 17. average amplitude of subject S4
Figure 18. average frequency for subject S4
Figure 19. percent time of 9-13 hz at 10-25 uV for subject S4
Figure 20. Percent time of 2-8 Hz for subject S4
Figure 21. Seizure rate during baseline (B), training (T), and follow-up (F) for subject S1
Figure 22. Seizure rate during baseline (B), training (T), and follow-up (F) for subject S2.
Figure 23. Seizure rate during baseline (B), training (T), and follow-up (F) for subject S3.
Figure 24. Seizure rate during baseline (B), training (T), and follow-up (F) for subject S4.
IV DISCUSSION

The results of this study lend additional support to the efficacy of EEG biofeedback for the reduction of epileptic seizure activity. The hypothesis, which stated that low amplitude training of 9-13 Hz would produce a greater seizure reduction than high amplitude training of 9-13 Hz, was confirmed by the findings of the review of the cases. Both subjects trained for low amplitude 9-13 Hz production (S3 and S4), experienced marked seizure reduction. Only one subject trained for high amplitude 9-13 Hz production (S1) experienced a seizure reduction. The other high amplitude subject (S2) experienced a seizure increase. Due to the fact that none of the subjects reached or maintained their amplitude criterion, it is not possible to attribute the seizure rate decreases to the production of criterion amplitude. Of the four parameters measured, none were consistently related either negatively or positively with seizure rate for all subjects. For this reason, each subject will be reviewed independently to examine the significant factors involved for that subject.

Based on Kaplan's (1975) normalization hypothesis, normalization of the epileptic EEG in relation to the parameters measured would vary from subject to subject. The basic concept would be to reduce slow wave and excessive fast wave activity while
increasing the mid-frequency activity. In addition, reducing high amplitude levels would also be considered a normalization. S1 experienced seizure reduction only after becoming discouraged and no longer attempting to produce higher amplitude levels. The resulting reduction of amplitude and percent time of 2-8 Hz could be considered a normalization of the EEG parameters for this subject. However, during other blocks of training similar reductions in both amplitude and percent time of 2-8 Hz did not result in seizure decrease. In addition, for S1 there were some suggestions from comparing blocks of data, that percent time of 2-8 Hz was inversely related to concurrent seizure rate. That is, when percent 2-8 Hz increased, seizure activity decreased. This is the opposite of what would be expected with normalization. Other EEG parameters did not appear to consistently change with seizure rate. Placebo effect could be offered as a rationale for the reduction however, due to the late onset of seizure abatement it appears unlikely. So for S2 there are no obvious factors relating to seizure reduction other than an overall decrease in percent time of 2-8 Hz and amplitude.

S2 represents a very difficult case to analyze. EEG parameters reflected very little learning, but two parameters varied consistently with concurrent seizure rate. Frequency varied inversely with seizure activity while percent time of 2-8 Hz varied directly with seizure rate. These two relationships were consistent with normalization. If normalization was important for seizure reduction it follows then that if S2 did not demonstrate improvement
In the seizure related parameters then seizure rate would not be expected to improve.

The reasons for S2's failure to improve EEG parameters appeared to be primarily psychological. For some time it had been observed that when S2 started to obtain a high degree of feedback, the amount of feedback would suddenly drop. Upon inquiry, S2 stated that she "was afraid of doing well with the feedback", and in general of being successful. In addition, S2 seemed to have a psychological conflict about reducing the seizure activity. Some short term counseling was conducted and was associated with a decrease in percent time of 2-8 hz and seizure activity. When it became obvious that long term intervention would be required, therapy was terminated and the subject was instructed to do her best. Percent time of 2-8 hz sharply increased, with a concurrent increase in seizure activity.

S2's reports of "aura" activity were highly subjective. External physical changes such as disorientation, changes in voice, body movement, facial expressions, etc., were never observed. Aura's reported during the biofeedback sessions did not produce consistent changes in the instantaneous EEG parameters. S4, who also reported very similar sensory experiences, produced an increase in high voltage, slow wave activity during a number of the reported sensory events in the lab. One explanation for this discrepancy might be that S2's focus for this activity is medial or in a different location than S4's and therefore more difficult to detect. It is also possible that S2's "aura" activity is more closely related to anxiety.
attacks than to partial-elementary seizure activity. S2 expressed a great deal of daily anxiety about a wide variety of areas. The subject, by self-revelation suffered from daily stress related headaches. "Aura" activity was reported to increase during periods of stress and high anxiety. S2 also attributed the reduction of complex-partial seizure activity, during the second month of follow-up, to practicing relaxation skills and graduation from college.

Because of the above stated psychological problems and yet the close relationship of two EEG parameters to seizure rate, it is difficult to determine the nature of S2's seizure activity. Long term psychotherapy and hospital seizure monitoring might be useful in clarifying this problem.

S3 experienced a rapid decrease in seizure activity over the first ten sessions. Placebo effect would be an obvious explanation for this decrease. However, seizure reduction was directly accompanied by a rapid decrease in percent time of 2-8 hz, amplitude and a sharp rise in frequency and percent time of 9-13 hz. These four changes approach normalization of the EEG parameters for this subject. Two parameters appeared to be closely related to seizure rate for S3. Frequency demonstrated an inverse relationship with seizure activity while amplitude varied positively. Both of these relationships conform to the normalization hypothesis. The overall reduction of percent time of 2-8 hz and increase in percent time of 9-13 hz are indications of normalization that correspond to the
overall reduction in seizure activity. During S3's relatively long seizure free period, he became complacent about producing feedback. As this progressed, S3's performance gradually deteriorated, as did the four EEG parameters. By the sixth block, percent time of 2-8 Hz and frequency had dropped. A burst of seizure activity followed this denormalization of the EEG parameters. Seizure activity again abated and was accompanied by an improvement of the EEG parameters.

During the second month of follow-up, seizure activity recurred and approached baseline levels. EEG data were not recorded during this period. The seizure increase supports Lubar's prediction (1980) (b) that seizure activity would return to baseline when biofeedback treatment was terminated abruptly. Each subject was encouraged to learn any subjective cues that might help identify correct EEG production and to practice this at home. Due to the subtle and obscure nature of the cues and S3's cognitive ability, proper home practice was deemed very unlikely.

As mentioned in the subject profile, S3 had neurosurgery to remove a right temporal subdural hematoma. Some of the results of the hematoma were a flattening of affect and a decrease in cognitive function. S3 was frequently non-responsive to verbal interactions, often inappropriate and always very slow. During training, S3 became much more alert, responsive and greatly increased the amount of appropriate verbal interactions. By the second month of follow-up, S3 had returned to the previous level of performance. These effects can be accounted for by considering the psychological reinforcement
of prolonged interaction with the experimenter and the experimental situation. However, a study by Woodruff (1975) suggests that the increase in frequency experienced by S3 might have increased the response time and thereby partially accounted for the improvement. No specific data exist to examine this possibility for S3.

It became obvious during seizure baseline that S4 was experiencing two basic types of seizure activity. The prominent variant during baseline involved complex-partial seizure, some of which generalized to full tonic/clonic seizures. Partial-elementary seizure activity comprised a small portion of the total activity. When S4 developed vertigo, the number of partial-elementary seizures greatly increased while the complex-partial/generalized seizure activity decreased. Over the course of the experiment, with other viral infections starting, partial-elementary activity soared. Comparison of the EEG parameters with the partial-elementary seizure rate indicated that there were no clear ties between changes in EEG parameters and concurrent partial-elementary activity. Some partial-elementary seizures which occurred during biofeedback sessions produced increases in high voltage, slow wave activity. The rise and fall of partial-elementary activity appears to follow the course of S4's series of viral infections.

Complex-partial/generalized seizure activity followed a different course than partial-elementary and appeared to be related to one of the EEG parameters. Comparison of the data suggest an inverse relationship between the percent time of 9-13 hz and
concurrent complex-partial/generalized seizure rate. This conforms to the normalization hypothesis. Other EEG parameters did not appear to closely relate to complex-partial/generalized seizure activity.

Overall, S4 experienced a marked increase in percent time of 9-13 Hz and a decrease in amplitude and frequency. Because of S4's high baseline average amplitude and excess of fast wave activity, all of these changes are considered normalization. Percent time of 2-8 Hz increased over the course of the experiment which would not be considered a normalization. By the final month of training both complex-partial/generalized and partial-elementary seizure activity had greatly decreased. During the two months of follow-up, both seizure rates continued to decline.

As mentioned in the subject profile, S4 experienced a long warning period prior to complex-partial seizure activity. S4 utilized this warning as a cue to apply the biofeedback skills. This occurred several times while in the lab. EEG parameters indicated a very high percentage of 2-8 Hz at the 100-150 μV level associated with the warning symptomatology (i.e., migrating severe head pain, olfactory and tactile sensation, buzzing noise, etc.). The first time this occurred (block 6) in the lab, S4 was unsuccessful at reducing the abnormal EEG activity and a generalized complex-partial seizure occurred. On two following occasions, S4 was successful at altering the abnormal EEG patterns, utilizing general relaxation and feedback without the theta alarm. In both cases, within 20 minutes, S4 had normalized EEG output, with an associated abatement of
pre-seizure symptomatology and aborting of possible seizure activity. These experiences were a major turning point for S4, who began to vigorously apply the techniques at home with a significant degree of success. S4 attributes the continued seizure abatement during follow-up to the acquisition and application of these skills.

Of the four subjects S1, S3 and S4 were highly motivated to reduce their seizure activity. These subjects were compliant and very cooperative during the entire experiment. S2 was also compliant, attending all sessions on time, maintaining a detailed diary, and proper drug levels. However, S2 never expressed a high degree of motivation for reducing seizure activity. Secondary gain appeared to be a major factor in this motivational problem. Secondary gains included reinforcement for maintaining the family role of the sick child and the use of epilepsy as a rationale for secondary psychological problems. For these four subjects it appears that motivation was a key factor for success of training.

For several years, the consensus has been that 12-14 hertz (SMR) was the effective factor in seizure reduction concurrent with biofeedback training. However, more recent opinions (Lubar, 1980 (a); Kaplan, 1980; Finley,1980) indicate that Kaplan's hypothesis of normalization is the most likely explanation for seizure reduction. The results of this study more closely support normalization than the stated hypothesis that amplitude is the critical factor in seizure reduction. While reduction of amplitude may be one component of normalization, amplitude reduction, in and of itself did not
consistently result in seizure decrease. However, each subject who experienced seizure reduction also experienced at least one component of normalization.

If these parameters are directly related to seizure activity, then it would be expected that a consistent and predictable change in seizure rate with each change in the parameter would occur. However, this was not the case. While some parameters indicated a relationship with seizure activity, none varied predictably 100% of the time. This could be an indication that there are a number of parameters for seizure activity and that it is the interaction of these parameters that results in abatement or exacerbation of seizure activity. By crude manipulation of several parameters, the ongoing interactions of all parameters are effected. The resulting indirect change, thus, effects seizure rate. This could account for why improvement in an important parameter does not always result in improvement of seizure activity. The improvement of one parameter does not mean that the total interaction of all parameters has equally or even significantly improved. This could also help explain why biofeedback training seemed to have a clearer effect on S4's complex-partial seizure activity and not on partial-elementary seizure activity. This rationale also suggests that complex-partial activity is effected by a different system of parameters than partial-elementary seizures. It also suggests that the manipulated parameters played a larger role in the total interaction of complex-partial parameters than in partial-elementary parameters.
And thirdly, the rationale suggests that for S4 partial-elementary seizure activity is more grossly effected by parameters of physical illness, stress or immunological parameters than are complex-partial seizures.

Why one parameter is more closely related to seizure activity in one subject and not in another is unclear. Selective attention may be playing a role in this phenomena. It could be that a subject is paying selectively more attention to manipulating one parameter than the others. Gercken (1978) demonstrated that 4 complex-partial epileptics could not simultaneously augment mid-frequencies and suppress low-frequencies. Rice (1978) suggested a "response differential", that is, at least for Gercken's subjects, it was easier to produce mid-frequencies than to suppress slow wave activity. If contrary "response differentials" existed in the subjects, then it could account for the variation in seizure related parameters among subjects. Rice (1978) is initiating some preliminary research to investigate this possibility.

It can only be speculated at this point how many parameters are involved in each seizure type and what their interactions are like. From this study it can be seen that parameters may involve slow wave activity, mid-frequency activity, amplitude, frequency, psychological factors, physical health and motivation. How these and other less obvious parameters interrelate is unknown. A great deal of research would be required to identify each parameter and its interaction.
Design criticism

The most prominent weakness of this study involved the lack of statistical data due to a small N. While this is by no means a new problem for biofeedback/epilepsy work, it remains a major stumbling block for determining possible cause and effect. Without statistical data to support or reject an hypothesis, no more than inferences or educated guesses can be made.

This study was also weakened by the lack of a post EEG and power spectral analysis to document any normalization of the EEG.

Amplitude shaping was a major weakness in the design of this study. Amplitude levels demonstrated a very high degree of variability from session to session for any one subject. Utilizing a standard operant shaping paradigm proved counter-productive for a parameter as highly variable as amplitude. A more successful approach would have been to set amplitude training levels at the daily amplitude baseline. Then shape toward the amplitude criterion from the daily baseline as opposed to starting from the amplitude level of the previous session as done in this study.

In addition, the Autogen 120A's feedback system was not well designed for training increases in amplitude. When the amplitude level was shaped upward, the volume of the feedback dramatically decreased. The volume range of the 120A was insufficient to correct for the decrease. This factor proved very discouraging as reported by some subjects.

While feedback volume could account for the problems of high
amplitude training, it can not account for the fact that neither of the low amplitude subjects (S3 and S4) reached or maintained the low amplitude criterion. One possible explanation might be that of differential attention to feedback. That is, the subject attended more to one component of feedback (pitch) than to another (volume). For example, due to the fact that S4 produced a high dominate frequency (11-12 hz) and its relative position within the 9-13 hz bandpass, high pitched "beepy" feedback was received. S4 spent a great deal of time attempting to reduce pitch and thereby make the feedback more consistent. This selective attention was at the expense of less attention being paid to reducing volume (amplitude).

**Future research**

A great deal of future research is needed in the field of EEG biofeedback for epilepsy application. Not only is there a need for rigorous scientific research, utilizing double-blind techniques, but also clinical research is needed. It has been fairly well documented that EEG biofeedback training can be effective for reducing epileptic seizure activity. It is now necessary to determine what components of biofeedback are effective for what types of seizure activity and to determine the basic mechanism involved. For example, if there are one or two critical parameters for each person, then it would be useful to determine if by training for only these parameters, seizure reduction could be obtained and if this reduction is faster or more complete than a less specific training paradigm.

Clinical research that is well documented is now needed. For
biofeedback to be useful it must be applicable in a clinical situation. The most effective clinical approaches, which reduce the amount of time, cost and seizure activity, need to be developed by systematic, well documented clinical applications. The present study is a step toward clinical application because it utilizes the type of equipment and basic approach that would be feasible for a clinician to apply. Future clinical research should concentrate on proper screening, short-term training techniques and the utilization of home training as a supplement to clinical training.
Appendix A.
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