THE CONTRIBUTION OF PSYCHOLOGICAL INTERVENTION TO THE MANAGEMENT OF EPILEPSY.

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A thesis submitted to the University of Glasgow in fulfilment of the requirements for the degree of Doctor of Philosophy.

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April 1988.

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ACKNOWLEDGMENTS.

The author would like to thank the following for their assistance with the work reported here:
Professor J.A. Simpson, Department of Neurology, and Professor D.N. Brooks, Department of Psychological Medicine, for their patient supervision of this work;
The Consultants in Neurology, Institute of Neurological Sciences, for access to patients in their care;
Mrs Janet Wilson, Paisley College, and Dr Adrian Bowman University of Glasgow, for Statistical advice;
Mr Charles Palliser, Department of English Studies, Strathclyde University, for help with spelling and punctuation.

SUMMARY.

The conventional treatment of epilepsy is pharmacological, but anticonvulsant drugs are not effective in every case and their use may be limited by side-effects. There are a wide range of psychiatric, psychological and social problems associated with epilepsy and it is argued that they frequently require intervention in their own right. There are many examples of psychological methods applied to seizure control in the literature, but unfortunately not all have adequate operational definitions and the application of such treatments has yet to be established.

A standarised interview schedule was presented to 105 consecutive patients with epilepsy attending neurology review clinics. The prevalence of psychological disturbance, in terms of standard scales, and poor seizure control, was measured. The proportion of patients experiencing various seizure related phenomena which might be of use in seizure interruption strategies was recorded. It is concluded that there are sufficient numbers of patients with refractory epilepsy and significant psychological disorder in this population for a treatment study to be viable.

The design of the treatment study is described. Two types of treatment are evaluated in a form of cross-over design. Treatment A teaches patients seizure interruption and

avoidance strategies. Treatment B focuses exclusively on alleviating anxiety and depression by standard psychological techniques. The main outcome measures are seizure frequency and scores on standard rating scales of anxiety and depression. The main purpose is to evaluate the effectiveness of these techniques in improving seizure control. The effect on psychological disorder will be also be assessed and an attempt will be made to identify factors predicting good and poor treatment outcomes.

Three groups of patients were studied. The first group (n = 19) had no significant psychopathology and received Treatment A only. The second and third groups, (n = 21, and n = 19) had both treatments administered consecutively. Group 2 had Treatment A then Treatment B and Group 3 B then A. Results showed a significant improvement in seizure frequency in all three groups after a stable baseline. Improvement was about 50% in 50% of cases and was maintained during six months follow-up. There was no difference between the groups in terms of outcome, no difference between the treatments and no treatment order effect. Groups 2 and 3 showed significant improvement in measures of anxiety and depression and all three groups showed a reduction in the numbers of work related and social activities they felt barred from as result of their epilepsy. It is noted, however, that at the end of treatment the overall mean weekly seizure rate is still above 2 and that score on anxiety and depression

scales remaons above 'normal'. Further analysis of the data shows evidence that anxiety, but probably not depression, may play a part in maintaining a high seizure frequency. It appears that depression is associated with lack of warning that a seizure is about to occur and with lack of independence, as defined in this study. Discriminant analysis showed that the best predictors of a good treatment outcome in terms of fall in seizure frequency, were presence of some form of warning of a seizure, and moderate pre-treatment levels of anxiety and depression.

The theoretical and practical implications of these results are discussed, with particular reference to possible treatment mechanisms. Some speculations which might explain the apparent relationship between anxiety and high seizure frequency are presented. It is concluded that psychological intervention has a potential application in the management of epilepsy but that future evaluations should use a longer follow-up period and should assess effectiveness of treatments when more than one therapist is employed.

CHAPTER 1

LIMITATIONS OF CONVENTIONAL MANAGEMENT OF EPILEPSY.

1. ANTI-EPILEPTIC DRUGS ARE SOMETIMES INEFFECTIVE.

2. ANTI-EPILEPTIC DRUGS HAVE SIDE-EFFECTS.

3. SEIZURES ARE NOT THE ONLY PROBLEM OF EPILEPSY.

The disorder of epilepsy is characterised by seizures. Conventional methods of treatment are directed at seizure elimination or reduction. The most effective anti-seizure treatments are pharmacological. Until the last decade the major emphasis of research in the area has been on the development of anti-epileptic drugs (AEDs), their optimal use with maximum effect and with the minimum of side effects. Epilepsy is not a single entity but rather a symptom of a great variety of underlying cerebral disorders. It is not therefore suprising that AEDs are more effective in some forms of the disorder than others. Generalised seizures, for example, can usually be controlled effectively by drug treatments, while temporal lobe seizures are quite frequently difficult to control. In many cases seizures can be virtually eliminated

without troublesome drug side-effects and without significant effect on life-style. However there is a significant sub-group of people with epilepsy for whom treatment based purely on pharmocalogical intervention is less than adequate. The following discussion considers the reasons for this.

1) ANTI-EPILEPTIC DRUGS ARE SOMETIMES INEFFECTIVE.

There may be a number of reasons why anti-epileptic drugs (AEDs) are ineffective in any given patient. It has been suggested that poor compliance is a major cause of refractory epilepsy (1), and that this problem is particularly prevalent in children (2) and adolescents (3). The latter authors, Friedman et al., suggest that non-compliance is related to adolescent striving for independence, but it must be imagined that poor understanding of the purpose of medication, and forgetfulness also play a significant part. Much emphasis has been put on the importance of monitoring circulating blood levels in recent years (4) and the need to improve compliance figures prominently among the reasons for this.

Giordani et al.(5,6) investigated the effects of intensive diagnostic and therapeutic intervention on a

series of patients with refractory epilepsy. Rationalisation of anticonvulsant therapy led to improvement in seizure frequency in 60% of their patients. It may be inferred from these studies that some cases of "refractory" epilepsy may be resolved by re-evaluation and improvement of clinical management.

However it has been asserted that 20 to 30% of all patients with epilepsy are refractory to anticonvulsant drug therapy, even when drugs are used in adequate doses and plasma levels are monitored (7). In simple terms epileptic seizures occur when the precipitating factors outweigh inhibiting factors. The mechanism of action of AEDs is generally that they increase seizure inhibition. There are a variety of ways in which this can occur and different drugs have different types of action. Phenytoin, for example, has been shown to stimulate the Purkinje cells of the cerebellum and by this means exert an inhibitory influence on the cerebral cortex (8), while valproate prevents spread of seizure activity and raises the threshold for firing of a focus (9). It may be assumed that any given drug will act in the same way on all individuals although individual dosage requirements will be a function of a number of factors (body weight, metabolic rate etc.) (10).

On the other hand, precipitating factors may vary greatly in type and significance from one individual to another.

Several types of metabolic derangement can increase seizure susceptibility, but which once detected may be rectified. These include hypoxia, hypoglycaemia, hyponatraemia, hypernatraemia, hypocalcaemia, and magnesium deficiency (11). In addition there are a number of non-pathological physiological states which may increase the probability of having a seizure, such as over-hydration, drowsiness, sleep deprivation and alcohol use (12). Specific auditory, visual and somatosensory stimuli can provoke seizures in susceptible individuals. There are rare reports of seizures being triggered by highly specific sounds such as the voice of a particular newsreader, frogs croaking and machinery droning (13). More commonly, light pattern changes caused by flashing lights, reading and moving grids have been shown to precipitate seizures (14). Cognitive events and emotional states have been frequently implicated but due to their subjective nature a direct association with seizures has been harder to prove (12, 15). Aird (12) concludes that there are over 40 known epileptogenic mechanisms, about 10 of which vary from hour to hour depending upon habit factors and the daily activities of the patients. In any given individual the probability of a seizure occurring will be a product of their innate seizure threshold, and the presence and strength of various precipitating factors to which they may be sensitive, countered by natural and AED induced inhibition. Given the complexity of this equation, and the potential for inter and

intra-individual variation, it is scarcely suprising that a significant proportion of patients is refractory to standard AED regimes.

2) ANTI-EPILEPTIC DRUGS HAVE SIDE EFFECTS.

Another important limitation of anticonvulsant therapy is that all AEDs in current use have significant side-effects (16). Consideration of haematological and hepatic disorders associated with these substances is beyond the scope of this text and they are, in any case, rare. However in an average epilepsy out-patient clinic there will be a minority of patients physically unable to tolerate AEDs in sufficient dosage to achieve satisfactory seizure control. Side -effects which are relatively harmless physically but psychologically distressing also occur. Phenytoin, one of the most commonly used AEDs, can cause unsightly facial hair growth, coursening of features and gum hypertrophy. (17) Sodium Valproate tends to cause weight increase (18). The psychosocial implications of these factors are apparent and may result in poor compliance.

There is increasing interest in cognitive side-effects associated with AEDs. Lennox and Lennox in 1960 (19) listed AEDs amongst the causes of mental impairment in patients with epilepsy, and suggested that phenobarbital

was responsible for worsening intellectual status in 12% of cases. It is probably true to say, however, that it is only in the last 15 years that cognitive effects of AEDs have been a major area for research. Possibly the work of Reynolds and Travers in 1974 (20) was seminal in generating interest in the area. In a study of 57 out-patients with epilepsy, they showed that after exclusion of cases with overt drug toxicity, patients with higher blood levels of phenobarbitone and phenytoin were more likely to show evidence of personality change, psychomotor slowing and intellectual deterioration and that this effect was independent of severity of the seizure disorder. At present the most commonly used AEDs are Phenytoin, Carbamazepine and Sodium Valproate. Phenobarbital, at one time ubiquitous, is used less commonly. There is evidence to suggest that all of these drugs can produce subtle cognitive impairment. Phenobarbital can impair short term memory and vigilance in normal volunteers (21) and reduce WAIS performance IQ in adult epileptic patients (22). Results of studies of the cognitive side-effects of phenytoin have been a little harder to interpret; some studies have shown that it can have a beneficial effect on some aspects of performance in non-epileptic subjects.(e.g Goldberg & Kurland 1970, (23) Smith and Lowry 1975, (24).) More recent work has shown that performance on tracking tasks, (25) and on visual vigilance tasks (26) improves with increasing circulating blood concentrations in patients

with epilepsy. However other studies have shown that there is an association between higher levels of phenytoin and poorer performance on tasks which have a strong motor element in epileptic patients (27). When Phenytoin has been compared to Carbamazepine it has been shown that it is associated with poorer performance on memory tasks (25). Carbamazepine has a relatively good track record compared to Phenobarbitone and Phenytoin, but MacPhee et al. have shown that it produces subtle psychomotor impairment in normal volunteers (28), in patients when it is administred in a single additional dose (29), and in patients on chronic Carbamazepine therapy (30). Sodium Valproate, the most modern of the major AEDs, appears to cause psychomotor impairment when high dose subjects are compared to low (31). There is also a single case report of "reversible" dementia where a patient with gross intellectual impairment improved following Sodium Valproate withdrawal (32). Clonazepam and Clobazam are benzodiazepines with anticonvulsant properties commonly used as an adjunct to other AEDs, but have been shown to produce impairment (33). The series of studies by Trimble and other authors has shown that multiple drug use is more harmful in terms of side-effects and probably not superior in terms of seizure conrol (34).

The point of listing these studies is to make clear the limitations of the use of AEDs; not only is there a risk

of potentially dangerous physical side-effects, but the mental efficiency of the patient is increasingly likely to be impaired with increasing dosages (4). Better seizure control may be associated with poorer quality of life as a result of subtle intellectual impairment.

3) SEIZURES ARE NOT THE ONLY PROBLEM OF EPILEPSY.

Aird (7), in his chapter on common sources of failure in the therapeutic management of epilepsy, is very forceful in pointing out the importance of attending to non-seizure aspects of epilepsy, although he is not the only author to express this viewpoint (35). "Another aspect of this problem (therapeutic failure) concerns the relative dichotomy of neurologic and psychiatric specialization in dealing with the complex medical, social and psychologic problems of epileptic patients. Too frequently, the neurologist tends to reduce the problem of diagnosis to seizure types, confirmation by EEG, and the prescription of appropriate drugs for the seizure types identified." Aird considers it essential that " the physician should have some understanding of the patient's personality and of how he functions in his family and environment. Sociologic and psychologic factors may equal or even outweigh the medical problem in importance, and the inadequate management of such factors may bias the patient's cooperation or response."

The literature dealing with the psychological and psychiatric problems associated with epilepsy is very extensive; having made the point that they are a major reason why management of epilepsy focused entirely on seizures is limited, a separate chapter will be devoted to their description.

CHAPTER 2

PSYCHIATRIC, PSYCHOLOGICAL AND SOCIAL ASPECTS OF EPILEPSY.

1. EPIDEMIOLOGY.

2. THE ROLE OF CEREBRAL PATHOLOGY.

3. PERSONALITY.

4. PSYCHOSIS.

5. DEPRESSION AND ANXIETY.

6. ATTITUDES AND PSYCHOSOCIAL PROBLEMS.

7. PSEUDOEPILEPTIC SEIZURES.

The literature dealing with each of these topics will be briefly reviewed. In each case there are implications for the present study and these will be noted.

1. EPIDEMIOLOGY.

Epidemiological studies of psychiatric disorders associated with epilepsy have given variable results,

depending on the operational definitions and the methods of data collection. Rutter, Graham and Yule (36), in their large survey of school children, found an incidence of 32% suffering from some form of psychiatric disorder amongst children with uncomplicated epilepsy. This was about 4 times the rate of the normal population in their sample. The prevalence rises to about 50% in epilepsy complicated by other neurological disorders, mainly because of mental subnormality. Pond (37) suggests that there are only two useful community studies of the adult population (38, 39); others are based only on in-patient data. In summarising the results of these two studies he concludes that the prevalence of general neurotic disorder is about 15-20%; approximately the same as in any sample of subjects suffering from any chronic medical disability. There is a further 15-20% who, according to Pond's definitions, suffer from "problems peculiar to epilepsy resulting from the associated CNS damage, drug effects and ictal alterations of consciousness." Within this group there is an increased incidence of paranoid hallucinatory psychosis. In real terms this means that of every patient with epilepsy attending general hospital clinics, or their general practitioner, 1 in 3 may have some form of psychiatric disorder; mainly conduct disorders in children and adolescents, and mild affective disorders in adults (40). A more recent, although rather small scale study is reported be Toone (41). His group interviewed 103 patients with epilepsy using the Clinical Interview Schedule (CIS)

(42), and found that the overall morbidity in terms of CIS scores was 48%, three-quarters of whom were diagnosed as having some form of affective neurosis.

These epidemiliogical studies serve to support the view expressed in the previous chapter; that psychological or psychiatric disorders are a very significant factor in epilepsy. This fact alone suggests that some form of psychotherapeutic intervention might contribute significantly to the management of the disorder as a whole.

2) THE ROLE OF CEREBRAL PATHOLOGY

One approach to quantifying and defining the relationship between epilepsy and psychiatric disorders is to attempt to relate the degree of psychiatric and psychological morbidity to variables which might give an indication of the severity of the seizure disorder. Some studies have shown that an early age of seizure onset is associated with intellectual deterioration (43,44), and Hermann et al (45) in a study using the MMPI, found that patients with adolescent onset of temporal lobe epilepsy (TLE) had a greater probability of developing psychological dysfunctions than patients with adult onset TLE. Seizure duration and absolute numbers of seizures have been shown

to correlate with degree of cognitive impairment (46) but not with psychosis (47). Dodrill (48) showed that emotional and psychosocial adjustment were worst in persons having large numbers of single convulsions and that a history of status epilepticus was associated with decreased neuropsychological and psychosocial functioning. Hermann (49) concludes that these last two factors are interrelated but that "further research is necessary to define the relationship." Despite the positive findings in this body of research Lesser, in his review of the evidence (50), points out that causal links between various seizure disorder severity factors, and psychological morbidity cannot necessarily be inferred since all may be a result of the underlying cerebral pathology. This point is also made by Engel et al (51) who conclude that not all of the behaviour disturbances of epilepsy are due to psychosocial factors; some may be a result of anticonvulsant drug use, and some to specific structural lesions. Beran and Flanagan (52), in a recent study comparing patients with and without structural lesions, concluded that the presence of such lesions was the key factor in producing psychosocial disability in a proportion of people with epilepsy.

A review of the literature leads one to the view that the causal relationships between the neurological, psychological, social and psychiatric aspects of epilepsy

defy disentanglement. Most discussion centres on the extent to which the various neurological factors directly produce psychological morbidity. Although some authors (48, 50, 53) briefly alude to the reverse possibility; that some types of psychological disturbance may increase seizure frequency or severity, this has not been considered an important line of research. However this possibility has exciting implications for treatment; not only are the psychological problems of epilepsy worth treating in their own right, but doing so might improve seizure control.

3) PERSONALITY

There has been much discussion of the concept of "epileptic personality". Since the disorder of epilepsy was first described it was thought that deterioration of behaviour and personality were inevitable (54). Gowers, (55) and others of his period believed the deterioration to be a consequence of seizures, but the work of Kraepelin (56) influenced opinion towards the view that epilepsy was a disease entity in its own right, which, as in dementia praecox, was genetically determined and led inevitably to a degraded state. By the middle of this century it was recognised that epilepsy is not a disease but a symptom of a great variety of cerebral disorders, some of which cause mental changes and some of which do

not. Epidemiological studies (37, 38, 39), were influential in moving epileptic personality research away from institutions, and the consensus of opinion of studies in the late 70's (57, 58, 59) was that there is no specific personality disorder associated with epilepsy.

There is some evidence, however, that there are particular behaviour or personality changes associated with temporal lobe epilepsy (TLE). These have been described very fully by Geschwind (60). In simple terms he considers them to be a result of a combination of "viscosity" of thought, hyperemotionality and hyposexuality. Geschwind and Bear and Fedio (61) relate these characteristics convincingly to the functions of the limbic system, and suggest that hyperemotionality, for example, may be a result of electrical stimulation of the limbic system and the surrounding cortex. This stimulation, arising from the epileptic focus, might lead to enhanced affective association with previously neutral stimuli, events or concepts, depending on the area of cortex being stimulated. Brandt et al. (62), in a study more carefully controlled than that of Geschwind since they also studied patients with generalised epilepsy, found that people with right TLE were indistinguishable from normals, in terms of the personality measures they used, and that patients with left TLE and patients with generalised epilepsy were indistinguishable from each

other. The latter groups did, however, show some of the characteristics described by Geschwind. Dodrill and Batzel (63) reviewed this confusing area and concluded that persons with TLE do not have a greater incidence of emotional and psychiatric problems than people with other forms of epilepsy, but that there may be some "behavioural peculiarities" which appear in a small proportion of people with TLE.

In summary it would appear that there is little evidence for the existence of an "epileptic personality". Although the behavioural characteristics occurring in a few patients with TLE may influence their treatment reponse it seems doubtful that this effect would be sufficient to justify attempts to measure personality factors in this study.

4) PSYCHOSIS

It is widely accepted that there is an association between epilepsy and psychosis. At one time it was thought that the two disorders were antagonistic to each other (56), and this belief was most influential in the development of ECT. This notion has fallen out of fashion although there are recent reports of patients without previous psychiatric history who developed acute psychotic states on establishment of seizure control and

EEG normalisation (64, 65). Reviews of the area (66, 67, 68) agree on the diversity of type of psychotic reaction in epilepsy. Psychotic symptoms may be directly related to seizure activity as in temporal lobe status, or may occur interictally. The clinical presentation of interictal psychosis is subtly different from non-epileptic psychoses (69) and much attention has been paid to the relationship between site of cerebral pathology and psychotic symptomatology (70, 71).

Detailed exploration of this area would be of little relevance to the present study for two reasons. Firstly, as will be demonstrated in subsequent chapters, overt psychosis is very rare in the population under study. Secondly patients with significant psychotic symptoms will almost invariably be receiving some form of psychiatric treatment. This treatment will not be standardised and so would confound the evaluation of a further psychological intervention. Patients with epilepsy and interictal psychoses might benefit from psychological intervention but would have to be studied independently from non-psychotic patients with careful control of their pharmacological and non-pharmacological psychiatric treatment. Given the relative scarcity of such patients this would have to form the subject of a separate investigation.

5) DEPRESSION AND ANXIETY

Depression and anxiety are very commonly reported by patients with epilepsy. At the University of Washington regional Epilepsy Centre, for example, over 40% of 211 adult patients stated that depression was frequently a problem "during the past month." (72), and in a community study carried out in London, 36% of the sample were diagnosed as having some form of affective neurosis (47). Yet Betts (73) comments that of all conditions associated with epilepsy, anxiety and depression are the least well recognised or described in the literature. As recently as 1985 Robertson and Trimble (74) claimed that theirs was the first therapeutic trial of the treatment of depression in patients with epilepsy. This is particularly surprising because since 1976 (57) it has been known that tricyclics and related classes of drugs tend to lower seizure threshold. In fact their claim was not quite valid; Davis et al (72) published some preliminary results of a study evaluating a cognitive behavioural treatment of depression in epilepsy in 1984, but the few authors who comment on anxiety and depression agree there is a need for further research into the nature and treatment of the non-psychotic psychological disturbances of epilepsy.

Betts (73) gives a useful descriptive classification of the ways in which depression and anxiety may be related

to epilepsy. They may occur as a reaction to the diagnosis of epilepsy and the psychosocial problems which frequently accompany that diagnosis. They may occur as a prodromal emotional change before a seizure. They may be experienced, in the case of TLE, as part of the aura or seizure itself. Both may occur in association with some form of interictal psychosis. Depression may occur as a result of a decrease in seizure frequency. Anxiety may present as a true phobic state, with seizures (collectively) as the unconditioned stimulus. There is also some evidence that panic attacks may share some underlying cerebral pathology with seizures; a case of panic attacks associated with a right temporal lobe arteriovenous malformation has been reported (75) and also folowing right temporal lobectomy (76). An investigative study by Coyle and Sterman (77) led them to conclude that a neurophysiological association between panic and seizures was at best very rare, but their study has been criticised on the grounds that not all their patients had EEGs and so seizures could not be absolutely ruled out (78). If underlying cerebral pathology is only rarely the cause of both seizures and psychological disorders another more direct causal link may exist between the two factors. Dowds et al. (79) observed that 72% of 300 unselected primary care patients with epilepsy reported that emotional upset was accompanied by an exacerbation in seizure frequency. It seems possible that emotional upset may lower seizure threshold. Although

this possibility has favourable implications for the usefulness of psychological intervention in seizure control other explanations for Dowds' observation exist. Patients undergoing some personal crisis are more likely to forget their medication and patients whose seizure control is deteriorating are more likely to become emotionally upset.

It is apparent from Betts classification, and the other evidence presented, that the types of anxiety and depression in epilepsy are varied, and the inter-relationships between the factors complex. Deciding if a patient is describing a surge of fear occurring as part of his seizure or in anticipation of having a seizure requires highly developed interviewing skills and clinical acumen. Similarly time and careful history taking are needed to distinguish a depressive illness requiring pharmacological treatment from feelings of helplessness and misery resulting from loss of social functioning. It is obvious that these disorders are of great importance among patients with epilepsy, and that some may well be amenable to standard, non-pharmacological psychological therapies. This, therefore is an indication of the type of therapeutic intervention which would be most worth evaluating.

6) ATTITUDES AND PSYCHOSOCIAL PROBLEMS

The psychosocial problems of epilepsy are very frequently referred to in the literature, but rarely defined. It is accepted that they are an important component of the disorder and that they require management in their own right (7), but little information is available on exactly how this should be done. However there is agreement that a major cause of the psychosocial problems is public attitude to epilepsy. Rutter, Graham and Yule (36) in their neuropsychiatric survey, concluded that "the widespread community prejudice against epilepsy was probably an adverse factor in the child's development and it may be one reason for the high rate of psychiatric disorder in the epilepsy group." A Gallup poll organised by Chanon in 1980 and quoted by Gunn (80) seemed to suggest that public attitude towards the disorder is becoming more tolerant. In 1979 5% of the sample felt that they would not let their child associate with an epileptic child; in 1969 the response rate to this question had been 15%. Burden, however, in a review of the social problems of epilepsy (81), states the opinion that this is an under-estimate of the likelihood of a negative reaction in a real life situation. He goes on to delineate the psychological effects of negative public attitude, namely a sense of inadequacy leading to social withdrawal or anti-social aggression, and the practical effects, namely difficulty in making friends and finding employment.

It is worth digressing to note that the origins of present day attitude to epilepsy are based firmly in our culture. Historically there has been a tendency to regard epilepsy as a disorder or disease which is in some sense visited upon the sufferer by an external agency. To the ancient Greeks, prior to Hippocrates, seizures were a manifestation of direct, divine intervention. Although in the fifth century B.C.E. Hippocrates ascribed epilepsy to a disorder of the brain, for many centuries the belief that epilepsy was caused, or at least regulated, by gods, demons or the movement of celestial bodies, persisted. Possibly the suddenness of onset of seizures, their dramatic and alarming nature and the fact that they frequently occur in individuals who are otherwise normal, combine to create an impression in the mind of the observer that something supernatural has occurred. In the thirteenth century Thomas Aquinas classified epilepsy among conditions of "natural" as opposed to "supernatural" origin, but even to the present day seizures provoke a sense of fear and people with epilepsy are frequently made to feel rejected by society (82). The importance of public education in dispelling the cultural myths which surround epilepsy has often been emphasised (82, 83, 7, 81, 84, 85, 86), but results of public opinion polls (94) and employment studies (87) suggest that this goal has yet to be achieved.

Pond (84), and more recently Gillham (85), draw attention to the importance of attitude to chronic medical disorder within the family. This may be distinguished from public attitude but may equally result in psychosocial difficulties. Parents may experience guilt if they believe epilepsy to be genetically determined, and also if they believe it to be a result of some trivial childhood accident for which they feel responsible. They may respond with rejection or denial of the disorder, or with over-protectiveness thereby fostering dependence and the sick role.

Attempts have been made to quantify the psychosocial aspects of epilepsy, most notably by Dodrill et al. (88), in the development of the Washington Psychosocial Seizure Inventory (WPSI). This 132 item questionnaire attempts to assess family background, emotional adjustment, interpersonal adjustment, vocational adjustment, financial status, adjustment to seizues and overall psychosocial functioning. The scale was correlated with professional ratings within each of the above sections. Validation of the scale (89), showed it to be, at the least, a reliable indicator of probable employment status. There are few references made to the WPSI in the literature subsequent to its inception in 1980, and so it might appear that it has limited practical application.

In summary there is agreement in the literature that one

of the major causes of psychosocial problems is the attitude of society, families and possibly patients, to epilepsy. Evaluation of some form of educative program in a clinical setting. aimed at dispelling misunderstandings about the disorder, would be useful.

7) PSEUDOEPILEPTIC SEIZURES.

Pseudoepileptic seizures are sometimes referred to as pseudoseizures, or psychogenic seizures, but in the view of Fenton (90) neither of these terms is adequate. The term "pseudoseizure" conveys the impression that the event is not really a seizure, while although it may not be aetiologically epileptic, it is undoubtedly a seizure. The term "psychogenic" leads to even more confusion but a useful definition is given by Fenwick (15). He defines primary psychogenic seizures as epileptic events triggered by an act of will on the part of the patient. It is not uncommon for patients to be able to induce seizures by attention to sensory stimulation (e.g. patterns of light) to which they are sensitive. Some patients report feeling that to have a seizure brings a sense of relief, and also security that the subsequent priod is likely to be seizure free. It is not uncommon to find patients who feel generally physically and psychologically better if they have an occasional seizure than if they have none. Obviously attention must be paid to these motivating

factors when attempting to eliminate primary psychogenic seizures. Fenwick defines secondary psychogenic seizures as those which are precipitated by a specific function of the mind without deliberate intent. By way of example he draws attention to the work of Ingram and Ryman (91) who described a patient whose seizures were precipitated by simple calculation. Both primary and secondary psychogenic seizures are epileptic in this definition. However Gumnit and Gates (92) the term "psychogenic" as though it were synonymous with "pseudoepileptic".

If the two disorders, epilepsy and pseudoepilepsy, were mutually exclusive then the management of both would be more simple. Riley and Roy (93), however, estimate that 26% of patients with epilepsy also suffer from pseudoepileptic seizures. It is not clear from their account how they arrived at this figure; Gumnit quotes estimates varying between 5% and 50% but points out that even the lowest estimate means that 350,000 Americans will experience pseudoepileptic seizures at some time in their life and that therefore the problem must be considered significant. Fenton (90) suggests that the reason for this frequency of the association between epileptic and pseudoseizures is that patients whose seizures come under pharmacological control have lost a valuable source of reinforcement. During the time that their seizures were not under control, particularly if onset was in adolescence, they may have missed opportunities for

developing socially acceptable sources of reinforcement and for acquiring stress coping mechanisms.

The reason for the large variance in prevalence estimates is that pseudoepileptic seizures are frequently very difficult to diagnose. Roy (94) found a personal or family history of epilepsy, or an experience of working in a medical environment, in about one third of a series of patients with hysteria, most of whom had hysterical convulsions. Thus simulated seizures may be very convincing in this population. Various authors have produced guidelines to aid discrimination between the two types of attack (90, 95, 92, 96, 97). The last three of these are based on studies carried out at the Minnesota Comprehensive Epilepsy Program. Gumnit (92) in reporting and reviewing the results shows that using multivariate discriminant analysis on certain clinical characteristics gives a classification rate of 4% false positive and 4% false negative.

Two recent developments have also proven useful in elucidating this diagnostic problem. Firstly EEG telemetry, allowing continuous monitoring of patients, has enabled seizures not accompanied by the expected EEG changes to be designated pseudoepileptic with some confidence. However a study by King et al. (98) highlights the limitations of this technique. In their study only 55% of the sample had seizures during prolonged monitoring,

leaving doubt as to the diagnosis in the remainder. In any case muscle artifact makes reading of the record difficult and the possibility that some patients may have had partial seizures causing electrical changes not detectable by scalp electrodes can not be completely ruled out. Secondly post-ictal rises in prolactin level have been demonstrated (99). This occurs reliably after generalised seizures and complex partial seizures, but not after pseudoepileptic seizures or simple partial seizures. It will be seen that a clinician who is able to put these diagnostic techniques together has a reasonable chance of being correct for most cases, particularly if the seizures are real or simulated generalised attacks. However it will also be seen that a possibility of mis-diagnosis remains particularly in patients with a combination of real and pseudo partial seizures. There are striking examples of misdiagnosis in the literature, Titelbaum (100) recently reported a case of pseudo-epilepsy who had had numerous admissions to hospital with presumed status epilepticus, and who eventually died of what appeared to be a miscalculated parasuicide attempt. On the other hand Herskowitz and Rosman (101) reported a case of "pseudo pseudo seizures" in a patient who reported faking seizures and who eventually proved to be suffering from genuine epilepsy.

The diagnostic problem is further complicated by the possibility of a neurophysiological or aetiological link

between hysteria and epilepsy. Trimble (102), in reviewing the evidence for such a link, concludes that "there is little doubt that patients diagnosed as hysteria very often have accompanying underlying neurological disease." He goes on to say that it appears possible that neurological disorder might predispose one to the development of hysterical symptoms and draws attention to the evidence that excessive AED use in epileptic patients can cause pseudoepileptic seizures, possibly by some disinhibiting process (103).

Once diagnosis of pseudoepilepsy has been made, and unecessary AEDs have been withdrawn leaving sufficient to control genuine seizures should there be any, there is still a formidable task ahead of the clinician. Fenton (90) reccommends a minimum of 10 and a maximum of 30 one hour psychotherapy sessions. He appears to envisage this taking place in an in-patient setting alongside a behavioural management or group therapy programme. He comments that work with the patient's spouse or parents is always required, and that after discharge from hospital contact with the therapist should be maintained at regular intervals gradually getting further apart for a minimum of two years. He also notes that the long-term outcome is unknown and quotes estimates of improvement rates which vary between 30 and 80%.

It will be seen from the foregoing discussion that the

incidence of pseudoseizures in an epileptic population is almost certainly too high to be a factor which can simply be ignored in a study of the effectiveness of psychological intervention in seizure control. It will also be seen, however, that diagnostic and therapeutic techniques would need to be elaborate and expensive if patients with pseudoepileptic seizures were to be excluded or treated.

CHAPTER 3

NON-PHARMACOLOGICAL METHODS OF SEIZURE CONTROL.

1. METHODS BASED ON LEARNING THEORY.

2. BIOFEEDBACK AND INHIBITION.

3. PSYCHOLOGICAL DISTURBANCE AND RELAXATION TRAINING.

A great variety of non-pharmacological methods of seizure control have been reported. For the purpose of this review they have been divided into three main categories but in almost every case the treatment in question could have been included in two or more categories. This is a major reason why the evaluation of these reports is difficult; in general it could be said that while their scope and variety is impressive, the elegance of their experimental designs is not. A general critique of the methodology of the studies discussed will be given in the final section, followed by a review of recent studies which overcome the methodological problems of earlier work.

1. METHODS BASED ON LEARNING THEORY

One approach to the management of seizures is to treat them as though they were simply undesirable behaviours. To do this would be to suggest that seizures are in some sense learned behaviours and that as such they can be extinguished. On this premise the whole range of contingency management techniques becomes available. It is hardly surprising that both patients, who experience seizures as an entirely involuntary event, and clinicians with understanding of the neurophysiology of seizures, regard this approach with scepticism. There are, however, many accounts in the literature of the effective use of contingency management techniques of seizure control. Mostofsky and Balaschak (104) in reviewing this area, quote studies in four categories according to the rationale behind the treatment. An example of the first of these, "denial of reward", in which the occurence of a seizure is not followed by a display of concern but is ignored, is found in a report by Gardner (105). He presents a case of a ten year old girl, who was having frequent seizures. "Frequent" is not defined, and the ambiguous term "psychogenic" is used to classify the type of epilepsy. The girl's parents were instructed to ignore seizures and to reinforce acceptable playing behaviour. Medication was withdrawn and in two weeks seizures ceased without further recurrence over a twenty-six week period. There is no information in this report which would lead one to suppose that this girl's seizures were not pseudoepileptic. However if only effective against pseudoepileptic seizures the

technique would be well worth developing.

Another type of contingency menagement programme is a "penalty programme". The paradigm for this is that the patient is made to enter a "time - out" room when having, or having had, a seizure. By describing this regime as a "penalty programme" Mostofsky and Balaschak carefully circumvent arguments about whether time-out rooms are punishment or merely denial of reward. They quote a sample case of a thirty-four year old male patient who had been hospitalised for fifteen years because of his low level of intellectual functioning and high seizure frequency. At base-line he was having twenty seizures per week. The time-out procedure was adopted and the number of seizures dropped to zero by the end of the first week. The programme was run for a further eleven weeks. During the subsequent five months he had only one seizure. Again there is insufficient information given to allow distinction between pseudo and genuine seizures.

Thirdly there are reports of techniques which might be described as relief avoidance programmes. In general an aversive stimulus, such as a shock or a foul tasting medicine, is given until the patient demonstrates reduction in the clinical or electrical manifestation of the seizure. Ounstead et al. (106), for example, administered a burst of subjectively unpleasant photic stimulation to a six year old boy when his EEG began to show pre-seizure changes. The

subject could terminate the unpleasant stimulation if his spike and wave activity stopped within five seconds of onset, and learnt to do so within a few trials. In this case it seems clear that the seizures were epileptic since EEG monitoring was used. The treatment mechanism, however, is less clear; the report might equally be an example of the use of biofeedback or of a seizure interruption technique. Both of these types of treatment are discussed in subsequent sections.

Wright (107) uses a punishment paradigm in the treatment of a 14 year old boy whose seizures were of "organic" origin. This method differs from relief avoidance. Instead of the subject being given the noxious stimulus until he learns to control his seizures to avoid the stimulus, the stimulus is given as an immediate consequence of the seizure. Under EEG monitoring this child was given an electric shock every time his record showed evidence of seizure activity. A reduction in frequency of 75% is reported.

Successful outcome single case studies where seizure free periods have been rewarded have been reported (108, 109, 110). A study of relatively superior design was carried out by Lavender (111). He carried out a series of four single case studies with adequate baselines and with a well defined treatment, the most important component of which was rewarding progressively longer seizure free periods. Two of his four mentally handicapped patients showed

significant improvement during the treatment phase of the experiment with reversal of the effect during withdrawal of reinforcement. It is not clear why treatment was not successful in the other two cases but this simple behavioural intervention certainly appears worth further investigation.

Systematic desensitisation is a treatment based on learning theory, widely used for treatment of phobic anxiety, in which the link between the stimulus and the phobic reaction is broken by systematic presentation of feared situations in a hierarchical order. Desensitisation has also been used to treat reflex epilepsy. As early as 1874 Dunsmore (112) described a patient in whom seizures could be triggered by pats on the head, but no attempts were made to habituate patients to seizure provocative stimuli until the work of Forster in the 60s and early 70s. Forster (113) described in detail the case of a 53 year old women who developed epilepsy two years after a head injury. She experienced brief focal seizures only while listening to the radio. Clinical tests showed definitive EEG changes in reponse to the voices of three radio announcers. Tapes of their voices were obtained and they were played to the patient for brief periods initially, and then for progressively longer periods until the threshold at which seizure activity began was determined. With repeated sub-threshold exposures the patient became desensitised to the stimulus and ceased to

have seizures. Forster has used this approach successfully to treat other forms of reflex epilepsy, such as reading epilepsy, and musicogenic epilepsy (114).

It is not necessarily clear from accounts of reflex epilepsy whether the stimulus is unconditioned or conditioned. In the former case underlying idiopathic neural susceptibility to the stimulus must be assumed. Photic stimulation is almost certainly an unconditioned stimulus to patients susceptible to its effects, although the mechanisms of epileptogenesis in photosensitive epilepsy are not completely understood (115). On the other hand an operant model may be applied to some sensorily triggered seizures. Chance association between a sensory stimulus and a seizure could conceivably increase the probability of a seizure occurring at the next presentation of the stimulus, perhaps as a result of the patient's expectations or apprehension. Although it is agreed that stress may precipitate seizures (116) the underlying mechanism is rarely discussed. Stress, or some of the physiological changes accompanying it, may be a primary unconditioned seizure trigger in some individuals, but the possibility that a learned association has occurred cannot be entirely discounted. Systematic desensitisation to stress provoking factors has been attempted in patients with epilepsy and is discussed in the final section which deals with psychological disturbance. However the fact that these treatments can improve seizure control adds little to

the understanding of the link between anxiety or stress and seizures.

2. BIOFEEDBACK AND INHIBITION.

These two techniques have been placed together because both require the subject to carry out some activity designed to inhibit seizure activity.

The principles which underly biofeedback have been succinctly defined by Lubar and Deering (117). "Biofeedback ..... is a methodology for acquiring control over internal processes based upon operant conditioning of electrophysiological, neuromuscular and autonomic activity. Procedurally, biofeedback requires that an exteroceptive stimulus is made contingent upon targeted biological activity. Ultimately control of targeted biological responses is acquired. The process may occur with or without awareness on the part of the subject as to exactly which manipulations must be done in order to bring about this control."

It is widely accepted that human and animal subjects can increase production of basic EEG rhythms if they are rewarded for doing so. The standard technique in human subjects is to transduce a selected frequencing band from conventional EEG output into an auditory or visual signal.

The subject is told to keep the signal on as long as possible. Subjects appear to be able to use this "feedback" to increase the period of time during which the selected frequency band is produced.

There is some evidence that this type of EEG biofeedback can improve seizure control. Cabral and Scott (118) trained three patients to enhance alpha rhythm and over a six month period observed a mean seizure frequency decrease of 92%, but they also used relaxation training and so it is not possible to identify the effective treatment component. Studies using direct feedback of seizure activity have not been promising (119, 120), but the use of feedback of the band of activity between 12 and 15 Hz, usually termed sensorimotor rhythm (SMR), seems to have some potential. This rhythm is found over the rolandic cortex when there is inhibitory activity in subcortical motor pathways. It is thought that SMR is generated by one particular pathway leading from the cerebellum to the ventral lateral and ventral anterior thalamus and thence to the sensory and motor cortex. SMR presents some technical difficulties for measurement because it can ride on a much slower "carrier" wave. Lubar has managed to overcome this difficulty and the subsequent studies use his technique. Sterman and his group first showed that cats could increase SMR if food rewards were made contingent upon it (121). They then showed, by administering Monomethylhydrazine that SMR trained animals had a higher threshold for seizures than control animals

(122). In a subsequent human study (123) they trained four patients to enhance SMR activity in response to visual feedback and reported, without statistical analyses, a 66% reduction in seizure frequency. They concluded that SMR must inhibit seizure activity. Following this Lubar and others devised sophisticated apparatus that reinforced SMR unless slow activity of 3 to 8 Hz was present because they believed that there was antagonistic action between these two rhythms. They used this apparatus in a series of systematic single-case studies (124, 125) and later in studies employing double-blind designs (126) comparing different reinforcement schedules and feedback frequencies ranging from 8Hz to 15 Hz. Total numbers of patients in this series are small; the most recent (126) used 4 males and 4 females, but the success rate appears to be unequivocal seizure frequency reduction in about 60% of cases during treatment and showing reversal during non-contingent feedback. In reviewing the series (117) Lubar concludes that training should take at least a year and that booster sessions will be necessary indefinitely. He reccomends that training should be carried out only by highly trained personel and preferably with relatively intelligent subjects.

Possibly the amount of time and sophistication of apparatus required has put researchers off because there are only two reports of the use of EEG biofeedback in seizure control in the literature after 1981. Tansey (127) reports a single

case study where SMR biofeedback was used in the treatment of petit mal epilepsy. The patient, a 14 year old girl, was given 33 sessions of SMR training and an increase in amplitude of 14Hz rhythm was observed. This was accompanied by a total cessation of seizures which had previously occurred at
a frequency of 4 to 5 per hour. A study using a new concept in biofeedback, "non-volitional" biofeedback, is reported by Ramamurthi (128). He and his co-author translated a range of basic EEG rhythms (usually alpha and theta), into visual analogues and fed them back to 58 patients with epilepsy so that they were made aware of when they were producing the particular rhythms. No instruction or reinforcement was given for producing any particular frequency. They report a reduction in severity and frequency of attacks of more than 80% in about a third of the cases, but the information given is too scanty for proper evaluation of the usefulness of the technique. It must be suspected that the complexity of the apparatus and the experimental situation led to a placebo effect in these subjects.

Per-cent end-tidal CO2 biofeedback has been successfully used in the management of epilepsy associated with hyperventilation (129). This training had a rapid corrective effect on respiration in a series of eleven women and seven men all with idiopathic epilepsy and chronic hyperventilation. For some reason data are

presented for only 10 subjects, but these showed EEG normalisation and a mean seizure frequency decrease of 48 per month. The authors suggest that treatment works simply by eliminating a seizure precipitating factor so significant in this group of patients that they were refractory to AEDs.

In summary there is evidence that EEG biofeedback can be used to train subjects to alter basic cerebral EEG rhythms and that this may increase seizure threshold or inhibit seizure propagation. Alerting subjects to EEG changes at seizure onset by sonding a tone or flashing a light may also be useful, but there is less support for this. Biofeedback has also been used effectively as a treatment for hyperventilation induced seizures. The main drawback of these methods is that they require much time, expertise and expensive equipment with the result that most evaluative studies have very small numbers of subjects.

"Conditioned Inhibition" is a term first used by Efron in 1957 (130), but he is not the first to describe a conditioned inhibition treatment. Gowers in 1881 (131) wrote about a patient in whom Jacksonian fits could be arrested by application of a ligature. The seizure began with a sensation in the foot which then passed up the leg. If a ligature was applied to the leg above the path of the sensation, the seizure terminated instead of progressing to

a generalised convulsion. After a few months the seizures spontaneously arrested at the spot where the ligature had been. Efron suggests that the ligature arrested seizure activity by "building up cortical inhibition", that is by causing a burst of cortical activity ahead of the path of the seizure. Thirty years later this explanation appears very simplistic, and indeed evidence has come to light which suggests that activity in an area of the cortex regularly involved in seizure discharges can actually trigger bursts of seizure activity (12, 15). Nevertheless there is nothing as striking in the literature as the case which Efron describes in two papers (130, 132) in support of his theory. His patient was a forty one year old female black American singer, with a seizure frequency of seven to eighteen per month over twenty six years. In the terminology of the time her seizures were classified as uncinate; more recent systems would term them temporal lobe seizures but they were invariably accompanied by secondary generalisation and were completely refractory to Phenobarbitone and Phenytoin. Diagnosis was confirmed by electroencephalography. All seizures followed an identical pattern; they began with a feeling of depersonalisation and frantic activity with excessive concern about time. This worsened until she experienced a "forced expectation of a strong smell", which eventually arrived "like an explosion" and which was "disgustingly sweet and penetrating". After about ten minutes she would feel compelled to turn to the right and a tonic-clonic seizure would ensue. It was

discovered that sniffing hydrogen sulphide before the actual olfactory hallucination, and during the "forced expectation" phase, invariably aborted the attack. If the gas was presented after this phase then bizarre fragments of the seizure still occurred. The number of occurrences of the initial phase of the aura was equivalent to the pre-treatment seizure frequency. Efron and his patient then experimented with different odours and discovered that provided it was strong and subjectively unpleasant any scent was effective. EEG monitoring confirmed that seizure activity began shortly after the patient reported a feeling of depersonalisation, and ended shortly after the administration of a strong scent. All anticonvulsant medication was withdrawn without effect. At this stage the patient was using a primary, unconditioned stimulus - the strong scent - to abort her attacks. The following year (132) Efron paired presentations of the scent with presentations of a silver bracelet. Eventually the sight of the bracelet alone was sufficient to terminate attacks, and so conditioned inhibition had been achieved. This was effective even during a continuous infusion of Metrazol. Until this point in the treatment seizure frequency had remained unchanged; there was no reduction in the number of auras although none progressed beyond the initial phase. After this point seizure frequency fell so that at the time of reporting the study the patient had been seizure free for 14 months.

Unfortunately, although Efron's studies cannot be faulted on methodological grounds and most be assumed to represent a real phenomenon, there have been no subsequent reports of a true "conditioned inhibition" treatment, or even of use of spontaneous unconditioned inhibition. This is surprising because patients experiencing olfactory hallucinations immediately before a temporal lobe seizure are uncommon but not rare. It should be perfectly possible at a large centre to evaluate a treatment similar to Efron's systematically.

The only other report of an attempt to interrupt the progress of seizures comes from Zlutnick and Mayville (133), but although their treatment was successful in 4 cases, they did not distinguish between behaviours which led up to the seizure and behaviours, or alterations in concious level, which were part of the seizure itself. Thus it is not clear whether their treatment inhibited seizures or eliminated precipitating factors.

Treatments using relaxation training may make use of some unconditioned inhibitory process but since other principles are involved they are discussed in a subsequent section.

3. PSYCHOLOGICAL DISTURBANCE AND RELAXATION TRAINING.

The relationship between anxiety and depression and epilepsy has already been discussed and it has been noted that many patients claim that these disorders can increase their seizure frequency, or bring about a breakdown of seizure control. (See Chapter 2 section 5). Treatment of these disorders, therefore, may be expected to improve seizure control in individuals who claim this association. Williams et al. (134) demonstrated the potential of psychiatric and psychological treatments in the management of epilepsy. In their series of 37 patients with refractory seizures 70% showed substantial improvement in seizure control after non-pharmacological psychiatric treatment and maintained this improvement during follow-up of 2 to 36 months. There are many rather serious methodological problems in this study; it is uncontrolled, treatments were not standardised, and some unknown proportion of the sample had pseudoepileptic seizures and not epilepsy. It is, however, most interesting to note in the light of Fenton's reccomendations (90) that treatment for pseudoepilepsy should take at least two years, that Williams achieved his results in only two sessions in some cases.

Other studies are better controlled, but are single case studies of highly selected patients and so generalisations about the potential application of the methods cannot be made. Standage (135), for example, presented the case of a 29 year old women with a seven

year history of both complex partial seizures and tonic clonic seizures, occurring at a rate of one per month, and according to her own account triggered by "tension". Her EEG was consistent with a diagnosis of epilepsy, but she had also been liable to panic attacks when left alone and had experienced extreme anxiety at the thought of going out. Initially relaxation was promoted with Diazepam and then relaxation training was substituted for the drug. A standard imaginal desensitisation procedure was carried out in seven weekly sessions and at the same time graded practice in leaving the house was implemented. The patient had only two seizures in the following year. The use of Diazepam spoils the design of the experiment because it has anticonvulsant properties, but the fact that the improvement was maintained after the drug was withdrawn certainly suggests that anxiety was a seizure precipitating factor and that its elimination was responsible for the improvement.

Other single case studies have been carried out by Parrino (136), and Ince (137). Parrino brought about a reduction in seizure frequency from 58 per day to none for 5 months in a 36 year old male with a putative diagnosis of Creutzfeldt-Jakob's disease. The main treatment component was deep muscle relaxation and this was used specifically to help the patient cope with anxiety provoking situations. Ince used a combination of relaxation training and desensitisation to treat an

anxious 12 year old boy with a combination of partial and generalised seizures. Again there was a striking reduction in seizure frequency - a fall from about 35 per week to none for 6 months after a 30 week treatment period.

Relaxation training has also been used in combibation with biofeedback by Cabral and Scott (118). The study is described in the previous section. Indeed it may be that relaxation and biofeedback are the same treatment. Lubar (117) suggests that relaxation enhances "idling" cerebral rhythms, such as SMR, and so may simply and cheaply achieve the same result as complex biofeedback programmes.

All the studies in this section, and indeed most of the single case studies in previous sections, can be faulted. Kraft and Poling (138) review all studies using any type of psychological treatment prior to 1982 and draw attention to the methodological problems. They point out that seizure frequency is always the main dependent variable, but that observational procedures are almost never adequately defined. Of the eleven studies examined only three employed an exprimental design adequate to demonstrate a functional relationship between treatment and changes in seizure frequency. They note that treatments are often poorly described and almost invariably cross the boundaries between theoretical

models. They conclude that "more carefully controlled research is necessary to demonstrate the power and generality of such teatments".

Since 1982 a number of researchers have taken Kraft and Polings comments seriously and produced larger controlled experiments. All of these can be included in this section since they use either relaxation training or some other treatment aimed at the alleviation of psychological disturbance. Chronologically the first of these investigates the effect on seizure control of relaxation treatment of stress (139). Rousseau et al. had a small sample, 8 subjects, but used a sham treatment to control for placebo effect. All subjects had at least six seizures during a three week baseline and were then assigned to a sham treatment condition or to relaxation training for three weeks. After this the sham treatment group had three weeks of treatment. Both groups showed a very significant reduction in seizure frequency during treatment but one subject showed an improvement during sham treatment and a reversal during real treatment. Although this study suggests that relaxation training can bring about a reduction in seizure frequency the baseline may be too short to rule out absolutely chance cyclical variations. The lack of follow-up does not allow comment on treatment effect maintenance. However, unlike most earlier studies, the treatment method is properly described and clear cut, and there is control for

non-specific effects.

The experimental design of Dahl et al. (140) improves on this; the baseline is longer (10 weeks) and there was a one year follow-up. Their subjects were 18 children, aged between 7 and 17 years, with refractory epilepsy, the treatment was composite, using contingency management, seizure interruption techniques and relaxation, and there was random allocation to "attention" control, and to no treatment control groups. The main dependent variable was the product of seizure frequency and seizure duration, termed "seizure index". Results showed a clear reduction in seizure index during treatment, maintained at follow-up and not reproduced by the attention control group. The authors conclude that their treatment programme may be effective for children with refractory epilepsy. The main limitations of this study are its small sample size (there were only six children in each group), and the composite nature of the treatment which prevents analysis of effective components. It must be imagined that when parents and teachers record seizure duration there must be considerable measurement error and possibly some bias. This factor may cast some doubt on the validity of the results.

Tan and Bruni (141) attempted to compare the effectiveness of a cognitive behavioural group therapy package with group supportive counselling. Their sample

contained 30 adults attending a specialist epilepsy centre. The study was well controlled with random allocation to the two treatment groups and to a third waiting list control group. Outcome measure included a range of psychological and psychosocial self report scales and ratings as well as seizure frequency. Results were disappointing; no significant differences were found between the three groups on any of the outcome measures except for therapist's global rating of psychological adjustment. Both treatment groups improved significantly on this but the control group did not. Since the ratings were not blind this result is not encouraging. Possibly group therapy is not suitable for this population where there are large individual differences in both seizure variables and type of psychological difficulty.

The most recent study, at the time of writing, was carried out by Dahl et al. (142). This study is broadly similar to the one carried out by the same authors in 1985 (139), but in this case their subjects are 18 adults instead of children and they effectively increase the sample size by giving some subjects two treatment conditions in consecutive phases. They simplified their treatment package to two main components; relaxation and ability to identify high seizure risk situations so that relaxation training could be applied appropriately. "Seizure index" scores were rejected in favour of a simple seizure frequency count. Results showed a mean

improvement of 66% during treatment which was maintained at 30 week follow-up. One suprising finding which the authors do not explain was an increase in seizure frequency of 68% in the group undergoing the "attention control" condition immediately after baseline. Although this study suggests that this type of treatment is promising, the authors point out that the sizes of the groups were minimal for statistical analysis, and that seizure frequency count is a rather limited outcome measure because it gives no indicaton of whether the patient is finding his seizures less troublesome, or if his level of psychological adjustment has improved. Although relaxation training is used invariably as a component of anxiety management programmes and although high seizure risk situations identified by Dahl's patients must provoke anxiety, the authors do not comment on possible relationships between anxiety levels and seizure precipitation.

At the end of this review it will be seen that the next logical step is to conduct a study using as large a sample as possible, prehaps more representative of the population of people with epilepsy as a whole. In most previous studies patients seem to be selected on the grounds that all else has failed.

All types of treatment discussed appear to have potential

but with the exception of Williams et al. (134) little attention has been paid to the possibility that psychological distress may maintain a high seizure frequency and that treatments aimed at alleviating it may improve seizure control. Possibly the recent work using relaxation training achieves its good results indirectly by improving psychological state. Use of a wider range of outcome measures might elucidate this.

The content of Chapter 2 was intended to drive home the point that there is more to managing epilepsy than reducing seizure frequency. The research reviewed in this chapter, with very few exceptions (134, 141) has focused exclusively on seizure reduction, thus falling into the trap so succinctly described by Aird (Chapter 1 section 3), when he points out the limitations of this approach. Future research should not only attempt to measure pre and post treatment psychological disturbance but should evaluate treatments designed to alleviate it.

CHAPTER 4

PRELIMINARY STUDY: CHARACTERISTICS OF AN OUT-PATIENT POPULATION OF PEOPLE WITH EPILEPSY.

1. INTRODUCTION

2. AIMS

3. METHOD

4. RESULTS

5. SUMMARY AND CONCLUSIONS

1. INTRODUCTION.

The literature review justifies the conclusion that there is a need for further evaluation of psychological treatments of epilepsy but the studies reviewed are very diverse both in terms of the treatments employed and in terms of the type of patient treated. Before any detailed plan of a treatment study can be made the target population must be selected and enough information gathered about it to allow a rational selection of an appropriate treatment.

The prevalence of epilepsy is estimated at 3 to 6 per 1000 population (143). The vast majority of people with epilepsy live at home; some attend specialist clinics; some are managed by their general practitioner; and presumably there is some unknown proportion who do not receive any medical attention. Although there is a higher incidence of epilepsy among people in institutions, relatively few people are institutionalised because of their epilepsy.

It is not proposed to make any attempt to evaluate psychological treatments as an alternative to pharmacological treatments; we are not therefore interested in patients with epilepsy whose seizures are well controlled on anticonvulsant medication. It is likely that most poorly controlled patients will either be institutionalised or will be attending specialist clinics. One possible study would be to evaluate systematically the effect of psychological teatments in an institutional setting and another in an out-patient population. In the light of the relative numbers of patients, and of current trends away from institutional care towards community care it seemed more appropriate to attempt to improve out-patient management of epilepsy.

It cannot necessarily be assumed, however, that patients attending specialist clinics for the management of their epilepsy require any treatment additional to that which

they receive as part of normal clinic routine. It may be that the combination of anticonvulsant medication and medical attention is sufficient to bring about a trend towards better seizure control in this population. Patients in regular attendance at specialist neurology clinics will already be receiving psychological support and possibly specific advice about psychological problems. Before embarking on a treatment study it is necessary to find out if there is any need for additional standardised psychological intervention in the target population.

Some knowledge of the type of problems and disabilities and characteristics of this population would make treatment selection more rational and efficient. If, for example, it was shown that most poorly controlled patients tend to be dependent on a relative, then it may be possible to make use of this fact to design treatment programmes which could be administered by relatives. If many patients have significant psychological disorders potentially treatable by psychological methods then it would be worth evaluating the effect of such methods on seizure frequency. If knowledge of seizure provoking factors and the use of natural seizure avoiding strategies are common, then evaluation of the effect of these features on seizure control must form part of the study.

2. AIMS

2. AIMS

The purpose of the preliminary study is to define and measure certain characteristics in the target population, as follows:

A. Measure seizure control.

i) Define "poor control" from the point of view of the clinician and of the patient. This will allow an operational definition for the purpose of subject selection in the subsequent treatment study.
If patients and clinicians are asked to rate seizure control, say on a three point scale from poor to good, then some measure of the severity of the disorder may be obtained. Severity and seizure frequency are not necessarily the same. Severity is a value judgement based on many factors probably differing in importance from individual to individual. Perceived control is a distillation of all these factors, unknown, guessed at and known. It may not be necessary to use both clinician and patient control ratings when selecting patients for the treatment study but it is worth establishing reliability by comparing ratings from two sources.

ii) Identify the proportion of patients attending neurology out-patient clinics whose seizures are poorly controlled in terms of the above definition.

B. Establish some measure of chronicity.

If poor control tends to be a temporary state rapidly alleviated by a change in medication, then psychological treatments have little to offer.

C. Define and measure the incidence of any co-existing psychological problems.

If it is shown that poorly controlled patients have an increased incidence of psychological disorders treatable by psychological techniques then it would be worth evaluating a treatment based on these techniques. The evidence that such treatments may improve seizure control has been presented in the literature review. In a carefully designed experiment it may be possible to generate and test hypotheses about the direction of causality between seizure frequency and psychological disorder, although it is unlikely, given the complexity of the relationship, that any definite conclusions will be able to be drawn.

D. Measure the proportion of patients who know of environmental or psychological factors which tend to

provoke seizures, and compare the incidence of these patients amongst those who are poorly controlled and those who are well controlled.

If it is shown that patients commonly know of seizure provoking factors, or can predict when they are going to have a seizure, it would suggest that it is possible to evaluate a treatment based on seizure interruption strategies.

If it is shown that poorly controlled patients know of seizure provoking factors less commonly than well controlled patients, this might be an indication that such knowledge is advantageous.

E. Measure compliance with anticonvulsant drug treatments.

Psychological intervention may be effective in some patients only because they respond to an increased amount of therapist time by increased compliance with drug treatments. It is therefore important to measure compliance before, during, and after psychological treatment.

F. Describe the demographic features of the population i.e age, sex, marital status, years since diagnosis, incidence

of medical and psychiatric problems, employment status.

These factors are of secondary importance and are unlikely to be of specific relevance. However since there is so little published information about patients with poorly controlled seizures it is necessary to eliminate the possibility that these factors are related to seizure control. Some information of practical use for treatment planning may emerge. Even with these variables included there are still others left out, for example, genetic and family history, educational history and drug history. It was decided that these would be so unlikely to be of relevance to the subsequent treatment study, or that it would be so difficult to obtain accurate records relating to them, that it would not be cost-effective to collect information about them.

3. SUBJECTS.

Subjects were drawn from attenders at Neurology review clinics covering two geographical areas. All patients had, in the view of the neurologist who interviewed them as part of the normal clinic routine, a firm diagnosis of epilepsy. The number of cases interviewed was 160. The schedule was completed by 105 patients; the remaining 55 were unable to supply all the required information. In some cases this was because a co-existing disability made sections of the interview irrelevant or inappropriate. In

some cases this was because patients did not know the answers to questions relating to their seizure type or frequency. This may have introduced a degree of sample bias since subjects who could not describe their seizures and did not know the frequency might have a less severe disorder. Since the main purpose of this preliminary study is to see if a treatment study is feasible, this type of sample bias, if it exists, does not pose any particular problem.

N = 160

Complete data on 105 subjects.

4. METHOD

Data were collected by means of a standardised interview and questionnaires (see appendix A). These were administered to consecutive patients in neurology out-patient clinics if they had a firm diagnosis of epilepsy in the view of the neurologist who reviewed them. This diagnosis was made from a combination of EEG and clinical evidence. Then the following variables were used in data analysis to meet the requirements of the aims of the study listed above.

A. DEMOGRAPHIC VARIABLES

A. DEMOGRAPHIC VARIABLES

i) Age.

ii) Sex.

iii) Marital Status.

iv) Employment.

This was assessed in terms of three categories:

1 = employed, 2 = unemployed for any reason except 3, 3 = lost job as a direct result of having epilepsy.

v) Medical History.

Patients were asked to list medical problems other than epilepsy for which they had received specialist treatment during the past year.

B. CLINICAL VARIABLES

i) Seizure Type.

Where possible this was obtained from the case file. Five categories were identified:

1 = major generalised

2 = partial seizures

3 = combination of 1 and 2

4 = 'Absences'

5 = Unknown

ii) Frequency.

Almost all subjects with frequent seizures had kept a written record of them from a period

varying from about a month to five years (one case). Patients with no written record were asked to estimate the average monthly frequency. A relative was asked to estimate seizure frequency independently. If agreement was obtained, and if this was consistent with reports in the case file, the estimate was accepted. If there was no such agreement the patient was asked to keep a written record over the next two months. It was not possible to obtain seizure frequency estimates by any of these methods for 9 out of the 160 subjects interviewed.

iii)'Control N'

The neurologist interviewing the patient rated seizure control on a three point scale:

1 = adequate

2 = inadequate but improved in last two months.

3 = inadequate

iv)'Control P'

As above but rated by the patient.

v) Chronicity.

Subjects rated as inadequately controlled were asked to estimate the number of months/years since they were well controlled. They were

asked to estimate the number of changes in medication in the last six months. The number of clinic visits in the last six months was obtained from the records.

vi) 'Years'

Number of years since diagnosis of epilepsy.

vii) 'Warning'

A yes/no response to the question of whether the subject experiences an aura or 'warning' that he is about to have a seizure.

viii)'Provocation'

A yes/no response to the question of whether or not the subject knows of anything which tends to provoke, trigger or bring on an attack. Subjects were also asked to list such factors.

ix) 'Repression'

A yes/no response to the question of whether or not the subject can ever put off or avoid having a seizure.

C. MENTAL HEALTH

i) 'GHQ 30'

The 30 item General Health Questionnaire was administered. This was selected as the quickest, most reliable and valid measure of significant psychological disorder.

ii) 'FSSI'

The Foulds Sign Symptom Inventory was administered to patients scoring above the criterion of 4 on the GHQ to enable some form of categorisation of psychological disorder. This scale was selected because it contains groups of questions designed to identify psychotic symptoms not included in the GHQ.

5. RESULTS

FREQUENCY AND CONTROL (AIM A.)

Figure 1. shows the distribution of seizure frequency per month over the sample of 151 patients from whom it was possible to get an acceptably accurate estimate. (see variable B ii). Fifty per cent of the sample had 5 or fewer seizures per month and the rest had from 5 to 160 seizures per month. The curve approximates to a Poisson rather than a Normal distribution, so that the lower the seizure frequency the larger the proportion of individuals suffering from that frequency.

[NOTE - Five patients had 50 or more seizures per month and these were excluded from further statistical analysis because of the unacceptable skew they imposed on the distribution. These 5 patients were similar in that they all suffered from very frequent 'absences' or 'petit mal' seizures. They were rated as poorly controlled but because their seizures were so brief and slight they did not appear greatly handicapped on any of the other measures.]

Table 1 shows the proportion of subjects in each of the three categories of control as rated by the neurologist (see variable B iii above), and the mean monthly seizure frequency in each of the categories.

Table 1

Neurologist's Seizure Control Rating (Control 'N').

	1 Adequate	2 Improving	3 Inadequate
N	42	39	65
Percentage	28.8	26.7	46.1
Mean Seiz.Freq. per month.	4.23	7.61	20.53

Table 2 shows the proportion of subjects in each of the three categories of control as rated by the patient

himself (see variable B iv above), and the mean monthly seizure frequency in each of the categories.

Table 2.

Patient's Rating of Seizure Control (Control 'P').

	1 Adequate	2 Improving	3 Inadequate
N	63	29	56
Percentage	43.2	19.9	38.3
Mean Seiz.freq. per month.	3.91	3.14	25.10

A chi-squared test comparing categorisation by the neurologist with categorisation by the patient gives a of 8.82, significant at the 2.5% level, thus demonstrating that the two measures are differently distributed.

T-tests comparing the mean seizure frequency in neurologist's categories with the mean seizure frequency in patient's categories, showed no significant differences.

It will be seen that either there is a very large amount of error in the Control measures or that patients and neurologists take factors other than absolute seizure frequency into consideration when rating control. Possibly neurologists and patients give different emphasis to the

various factors involved in making a control rating, but the result is that some patients believe themeselves to be adequately controlled when the clinician reviewing them does not. This serves to show the subjective nature of seizure control assessment, and that it does not depend simply on a frequency count.

CHRONICITY (Aim B.)

Fifty one patients were classified as poorly controlled by both the clinician and by their own rating. Amongst 28 of these the mean time since control had last been adequate wsa 2.1 years with a range of 8 months to 10 years. The remaining 23 patients said that control had never been adequate since they first began to have seizures.

The number of changes in anticonvulsant drug in the previous six months amongst the 51 poorly controlled patients ranged from of 0 to 4.
The mean number of changes in dosage was 5.3 with a range of 0 to 10. The upper limit of this range is rather approximate because most patients who had had more than 2 or 3 changes in dosage were unsure as to how many. Case records were not helpful because some changes had been instituted by the patient's G.P.

The mean number of times poorly controlled patients had

been reviewed during the previous six months was 2.1 with a range of 0 to 8.

Twenty patients had had no change in medication and had not been reviewed during the previous six months.

There are a number of implications from these data concerning frequency, control and chronicity for the proposed treatment study:

1) It will be possible to obtain a sufficiently large number of subjects who have seizures frequently enough to make treatment evaluation possible over a matter of months rather than years.

2) There is a large enough sample of patients with high seizure frequency who are rated as poorly controlled.

3) Control ratings and seizure frequency appear to measure different aspects of control. A measure of frequency and a control rating should be used in selecting patients for the treatment study.

4) Poor control appears to be a relatively stable state. These data tend to support the suggestion in the literature that there is a distinct sub-group of patients

for whom conventional treatment is not effective.

5) Changes in medication in this population are not infrequent and the effect of this will have to taken into consideration in an evaluation of the impact of psychological treatments. However should this prove to be too complex there would probably be enough patients whose medication would not be changed during the course of the study to allow the exclusion of those whose medication was changed.

The importance of these implications is apparent; the treatment study would be less tenable if, for example, seizure frequencies were so low that the study would have to take place over a period of time which was longer than the average period during which seizures stayed poorly controlled without psychological treatment. It is essential that control should be rated as poor, as well as that seizure frequency should be 'high'. 'High' is an arbitrary term. A patient with 20 seizures per month who rates his control as adequate and whose neurologist agrees with him, does not require intervention. A patient with 10 seizures per month may be considered very poorly controlled and be a good candidate for treatment.

PSYCHOLOGICAL MORBIDITY (Aim C.)

The measure of 'psychological morbidity' in this part of the study is the GHQ 30. This measure is not an aid to diagnosis of the specific psychological problem, but is an indicator of severity. As a research tool it is ideal for the present purpose which is simply to identify psychological morbidity in the target population.

Mean GHQ score was 6.81 with a range of 25 and standard deviation of 6.52.

When using the GHQ 30, a score greater than or equal to 4 is generally taken as an indicator of significant psychopathology. In this sample (N = 105) 56.6% scored above the cut-off point. In Goldberg's sample of 4067 primary care attenders 38.8% scored above the cut off point. It would appear that compared to Goldberg's sample this sample experiences significantly more symptoms of anxiety and depression. However such a comparison is not really possible because certain items in the GHQ confound the feelings associated with seizures with those associated with anxiety. Thus the GHQ score may be slightly artificially raised. Comparisons within the sample might also be affected by this problem; an individual with an improving seizure frequency could score lower on the GHQ simply because he has less somatic disturbance with the decrease in seizures. The effect of

this artefact would be small and does not invalidate use of the GHQ but it should be borne in mind to add a degree of caution to any conclusions drawn.

The Foulds Sign Symptom Inventory was administered to give some indication of diagnostic type in terms of psychological disorder. It was administered to the first 20 consecutive patients and then to patients who scored above the cut-off point on the GHQ. Among the first 20, 12 scored below the GHQ cut-off. Of these, 7 checked no items at all on the FSSI and the remainder not more than 2 items. Of the 80 who completed the FSSI only 5 patients checked more than 2 items on the 'psychotic' scales. The rest all checked at least 3 items on scale A (anxiety) and scale B (neurotic depression). The high correspondence of significant GHQ score with the A and B sections of the FSSI supports current thinking that anxiety and depression form a significant part of the psychopathology measured by the GHQ.

The correlation coefficient (Pearson's r) between 'GHQ' and 'seizure frequency' is 0.34 with $p < 0.0001$.

Thus in statistical terms there is a very highly significant relationship between psychopathology and seizure frequency. The clinical significance of this relationship is less impressive. Even if we assume that there is no measurement error and that there is a direct

causal relationship between GHQ and seizure frequency thus:

GHQ score $\longrightarrow$ seizure frequency

then the best that a total zeroing of GHQ could achieve would be an 11.8% reduction in seizure frequency. It must also be borne in mind that since GHQ is not an interval scale a Pearson's correlation is not a precise measure. It may fail to identify distinct sub-groups. However the plot of GHQ against seizure frequency from which the correlation was calculated showed a relationship which, allowing for wide scatter, was approximately linear with no clusters at either end of the scale. Thus it may be assumed that there are no identifiable sub-groups.

The implications of an examination of psychological morbidity in this population are:

1) that there is significant psychopathology in this population,

2) that allowing for the limitations of the FSSI the psychopathology is non-psychotic and may be amenable to psychological treatment,

3) that treatment of psychopathology could not cause more

than an 11.8% reduction in seizure frequency; indeed since this estimate is based on two rather gross assumptions the actual effect is likely to be far less.

'AURAS', 'TRIGGERS' AND SELF-CONTROL (Aim D.)

Table 3 shows the proportion of subjects who experience some warning or 'aura' before a seizure, the proportion knowing of some psychological or environmental factor tending to provoke seizures and the proportion who feel that they can exert some self-control over seizures.

Table 3.

Proportions of Subjects Experiencing Seizure Related Phenomena.

	YES	NO
AURAS	N = 66 % = 62.9	N = 39 % = 37.1
TRIGGERS	N = 69 % = 65.7	N = 36 % = 34.3
SELF-CONTROL	N = 16 % = 15.2	N = 89 % = 84.8

Of the 66 patients aware of 'auras' 41 also claimed to know of provocatice factors, or 'triggers'.
Of the 69 patients who claimed to know of factors triggering seizures 54 named 'anxiety', 'tension' or 'worry'. Other factors, with one or two unique exceptions,

were excitement or rage, or were related to the menstrual cycle, sleep patterns or diet.

T- tests showed no significant differences in seizure frequency between the subjects experiencing these factors and those who do not.

It would appear then, that knowledge of provocative factors, presence of auras and belief in one's ability to exert some control over seizures confer no special advantages. However none of these patients had ever had any instruction concerning the use of these factors in interruption strategies and the apparent lack of advantage should not deter systematic investigation of such strategies. It is promising that the most commonly encountered provocative factors are manipulable by psychological means.

COMPLIANCE (Aim E)

Sixty five patients claimed that they always took their took their medication exactly as prescribed. Twenty seven said that they occasionally missed a dose, nine said that they frequently forgot their medication and the remaining four said that they deliberately took less than the prescribed dose. An examination of the case records showed that eleven patients had drug levels below the therapeutic range when last tested.

It will be beyond the scope of this study to monitor drug levels at regular intervals during psychological treatment and follow up. Some control over this problem may be achieved by excluding patients with a history of poor compliance and/or by giving patients firm advice to comply with medication well before the start of treatment, so that any improvement achieved by this can be measured independently from other treatment effects.

DEMOGRAPHIC VARIABLES (Aim F.)

AGE Mean 33.01 yrs. Range 16 - 62 S.D. 12.58

YEARS SINCE DIAGNOSIS Mean 17.66 yrs. Range 0 - 57 S.D. 12.35

Sample contained 51 males and 54 females.
50 were married, 52 single and 3 divorced.

There was no significant correlation between Age or Years since diagnosis and seizure frequency.
T - tests showed that neither age nor sex is related to seizure frequency. It may be concluded that there will be no particular demographic sampling bias when selecting poorly controlled patients for the treatment study.

Age at onset might have been a more significant measure

than years since diagnosis and patients were asked to give this (see Appendix). However such a large proportion of patients thought that they might possibly have been experiencing seizures for some years before diagnosis that this measure was rejected in favour of years since diagnosis since the latter was more certain.

SEIZURE TYPE	1. Major Generalised.	N = 14	13.3%
	2. Partial	N = 44	41.9%
	3. Combination of 1 and 2	N = 26	24.8%
	4. Absences	N = 12	11.4%
	5. Unknown	N = 9	8.6%

Seizure type is biased towards categories 2 and 3 relative to estimates of seizure type in the general population. Category 2 includes all types of partial seizure and category 3, mixed partial and generalised. The bias will be due to the fact that partial seizures tend to be more difficult to control and thus patients suffering from them are more likely to be attending specialist clinics. This bias might have some implication for treatment selection - there is more prospect of using interruption strategies with patients suffering from partial seizures than with those suffering from generalised seizures because the former may experience auras.

EMPLOYMENT

1. Employed	2. Unemployed	3. Unemployed as a result of epilepsy.
N = 34	N = 35	N = 36
32.4%	33.3%	34.3%

Unemployment rate is higher than in the general population (categories 2 and 3). An attempt was made to ascertain the importance of this factor by further analysis of the relationship between employment and seizure frequency. GHQ was included in the analysis because it is likely that unemployment may influence score on this measure; it has already been observed that a relationship exists between GHQ and seizure frequency.

Table 4

Relationship between Employment, GHQ and Seizure Frequency.

	EMPLOYED	UNEMPLOYED	UNEMPLOYED AS A RESULT OF EPILEPSY
Mean GHQ	4.47	5.29	10.50
Mean Seiz.Freq. per month.	15.59	8.43	13.33

$F = 6.50$ (d.f. 2,104) $P < 0.01$
$F = 4.34$ (d.f. 2,104) $P < 0.01$

Examination of cell means shows that patients in category 3, those who have lost their jobs as a result of their epilepsy, are very much more psychologicaly disturbed (in terms of the GHQ) than those in the other two categories. Yet employed patients have slightly more seizures per month than those who have lost their jobs. The sociological implication is that actual frequency of seizures has nothing to do with ability to hold down a job. There is also an important implication for the treatment study. If the high GHQ score is the result of becoming unemployed then psychological techniques may not have much to offer in terms of reducing GHQ score. If patients are more likely to become unemployed if they are suffering from the type of psychological distress which leads to high GHQ scores then alleviating this might increase the probability of gaining employment.

MEDICAL AND PSYCHIATRIC MORBIDITY.

Twenty-three out of 160 patients had a medical disabilty in addition to their epilepsy which made it impossible for them to complete the interview and questionnaire schedules. In some cases this was a direct effect of the condition as in the case of blindness or mental handicap. In other cases their condition made interpretation of results impossible. Examples are a patient with a very high score on the GHQ who was concerned about his recently diagnosed Parkinson's disease and a patient with poorly

controlled diabetes who could not distinguish seizures from hypoglycaemic attacks. It was decided that such patients should be excluded from the treatment study because of the risk of extraneous factors confounding outcome evaluation.

Eleven patients out of 160 were undergoing psychiatric treatment, 3 of these had significant scores on the FSSI 'psychotic' scales and so did 2 others not attending a psychiatrist. Eight of these 13 were classified as poorly controlled by themselves and by the neurologist who reviewed them. It was decided to exclude patients who were undergoing psychiatric treatment; there are too few of them to allow them to be studied as an identifiable sub-group, but enough of them to confound results when evaluating psychological treatments which might have some overlap with psychiatric treatment.

5. SUMMARY AND CONCLUSIONS

The field study has demonstrated that in the target population - attenders at neurology out-patient clinics - there is a sufficiently high proportion of patients with chronically poorly controlled seizures to make a treatment study methodologically possible and worthwhile.

An examination of some of the characteristics of this

population has shown that about half of them have significant scores on the GHQ 30. The implication of this is that many might benefit from psychological treatments of anxiety and depression. There is a significant relationship between GHQ score and seizure frequency but it is too small to offer much hope that treating anxiety and depression will have much impact on seizure control.

About two thirds of the sample experience some warning of a seizure and about two thirds know of factors tending to 'trigger' seizures. This indicates that it will be possible to evaluate methods which rely on these factors, but the fact that they are equally distributed across the range of seizure frequency suggests that they carry no natural advantage for seizure control.

CHAPTER 5

TREATMENT STUDY: DESIGN AND METHODS.

1. TREATMENT SELECTION

2. TREATMENT PROCEDURE

3. PATIENT SELECTION

4. EXPERIMENTAL DESIGN

5. OUTCOME MEASURES

6. PROCEDURE

1. TREATMENT SELECTION.

A review of the literature shows that there is quite a variety of possible treatments which can loosely be termed 'psychological'. There is sufficient evidence that psychological intervention can be effective in seizure reduction for this to be undisputed. What is less certain is how wide is the application of these methods.

Systematic comparison of treatments has not been carried out and so potentially any one or any combination of several might be an equally good choice. The preliminary study has given some further indication of what would be appropriate and practically possible in an out-patient population.

Theoretical Considerations.

One treatment which is promising in terms of its potential for an out patient adult population is one which teaches subjects to avoid seizures or to interrupt or abort them. The preliminary study shows that 62.9% of patients experience an 'aura' or some warning of an attack; that rather fewer (15.2%) think that they can sometimes suppress seizures; and that 65.7% think that they know of some factor or factors which provoke seizures. In the preliminary study sample the presence of these factors does not necessarily lead to better seizure control.(see section on results of preliminary study) It is hypothesised, however, that these factors might form a potential natural resource. It is only a minority of patients who believe that they can exert some control over their attacks and none in the sample used for the preliminary study had ever tried to make use of these factors in a systematic way. Some exhibited almost superstitious behaviour in attempts to avoid seizures but

these attempts tended to be short lived and not logically organised. A treatment which uses the techniques of behavioural analysis to identify factors which provoke seizures, and evaluates various interruption strategies in a systematic, experimentally based way might be able to make use of this "natural resource".

During pilot experiments with psychological methods it was observed that some patients who do not spontaneously report seizure warnings or triggers may develop them or become aware of them with psychological intervention. 'Auras' are part of the seizure itself, and may be sometimes very short, but in pilot experiments some patients reported that auras became longer with attempts to interrupt them. These observations suggest that it is worth trying interruption and avoidance strategies with all patients.

Results of the preliminary study show that a large proportion of the target population is suffering from significant psychological distress, usually in the form of anxiety and depression. Most patients believe that stress or anxiety increases their seizure frequency. There is a significant correlation between seizure frequency and GHQ score in the target population. The problem of establishing causality has been discussed in a previous section, and it was noted that the shared variance between seizure frequency and GHQ was only 11%, but treatments

aimed at reducing anxiety and depression are obviously desirable for two reasons. Firstly patients will benefit from reduction in psychological symptomatology even without improved seizure control, and secondly if the result of treatment is improved seizure control, then we have sound experimental evidence that anxiety can have an adverse effect on seizure control, even though that effect may be small.

During data collection for the preliminary study it was observed that a large proportion of patients over the whole range of control felt that they had been given inadequate information about the nature of epilepsy. It is possible, although no actual evidence is available to support the notion, that education and the dispelling of certain misconceptions about the nature of the disorder, (e.g. that it leads to inevitable deterioration) might have a therapeutic effect.

Practical Considerations.

Information from the preliminary study indicated a number of practical considerations which should be taken into account in treatment selection. Most people with epilepsy live at home; and some never attend specialist clinics. The ones that do so are likely to be patients with the more difficult problem, either because there is some other

complicating factor, or because their seizures have proved difficult to control. It is this latter group which is the prime target of this study. Since they are an out-patient group, out-patient treatments will be the cheapest and most practical. Thus treatments should be to a large extent self-administered to reduce numbers of treatment sessions, and viable with or without the support of a relative. Intensive behavioural modification programmes or biofeedback programmes are therefore not a practical option.

The number of attendances should be as few as possible, because firstly, as shown in the preliminary study, a proportion of patients are working and their work situation may be already rather precarious; secondly some can only leave the house if accompanied by a relative, and thirdly the geographical area covered by specialist clinics is large and so some patients in the target population will have to travel considerable distances.

The preliminary study revealed that the number of patients who might potentially benefit from treatment is large. If treatment methods are kept as simple as possible then once evaluated they need not necessarily be administered by clinical psychologists. It may be possible simply to standardise advice, information and instructions which are already given as part of routine clinic practice so that no extra input would be required. Diversification of

therapists would allow larger numbers of patients to be offered 'psychological' intervention. The disadvantage of minimal intervention out-patient treatments is , of course, that they rely heavily on patient motivation and belief in the techniques suggested. If the treatment appears bizarre, or if the patient has a long history of expectation of a pharmacological "cure" then maintaining compliance will require considerable expertise on the part of the therapist. Where the success of a treatment stands or falls on the therapist's ability to sell it, there is a risk that success rate will diminish with diversification of therapists. Future research should examine the effectiveness of treatments when carried out by a range of therapists from different professional backgrounds, but at the present time the aim is only to evaluate effectiveness of treatments administered by one psychologist. The disadvantage is that it will be difficult to control for so called "therapist variables." Treatment success, if there is success, may be dependent on some unmeasurable selling ability of the therapist carrying out the present study.

The main practical considerations, therefore, are that treatments should be simple, relatively short, and consist essentially of information and techniques that patients can learn and apply for themselves.

2. TREATMENT PROCEDURE

In the light of the above considerations the following two treatments were employed in the study, each being independent of the other. Three blind raters observed a total of ten treatment sessions between them and identified correctly which treatment was being used in each case.

Treatment A: Education, Avoidance and Interruption.

This treatment required a detailed account from the patient, and where possible a relative, of any physiological or environmental factor which he/she thought might provoke seizures, either immediately and directly, or indirectly. The most commonly mentioned factors were tiredness, lack of sleep, too much sleep, alcohol abuse, hunger and hot rooms. Most patients also mentioned psychological factors at this stage, but great care was taken not to comment on, or to allow discussion about these. Instead a practical discussion was held which dealt with changes in life style which would enable the patient to avoid these physiological or environmental provocative factors.

The patient and someone who had observed some of the patient's typical seizures were asked to provide a

description of them, with particular emphasis on sensations and movements in the initial stages of the attack. The patient was then advised to try to carry out some activity counter to the normal initial stages of the attack. If patients had tried this sort of strategy before, they were encouraged to make a further more systematic attempt, as described below. Many patients felt that their previous efforts had been "silly" because they tended to believe that seizures were something which "just happened". They were discouraged from this view and were given examples of patients in whom such techniques had been successful. The nature of epilepsy and seizure proneness was explained to them. Patients were encouraged to ask questions and these were answered factually.

In the case of seizures beginning with some limb or body movement, the patient was advised to prevent or to counter this movement.

In the case of seizures beginning with a hallucinatory sensation the patient was advised to "flood" the relevant sensory system with some real stimulus. Olfactory hallucinations, for example, can sometimes be countered by sniffing some strong perfume.

In the case of seizures beginning with some forced thought pattern the patient was advised to impose some semi-automatic cognitive activity, such as counting in

threes or reciting poetry.

In the case of seizures beginning with an epigastric sensation, or some undescribable "funny feeling", the patient was advised to take in a deep breath and let the air out very slowly, relaxing as much as possible.

Relatives were asked to remind the patient about the proposed strategy, particularly when they observed that the patient was about to have a seizure. If it was clear by the next treatment session that the strategy was not working then some modification was suggested.

It will be observed that Treatment A. is essentially three treatments, one educational; one concerned with avoidance of provocative factors; and one with interruption strategies. The disadvantage of this is that it will be impossible to evaluate the three aspects independently. The advantage is that it will allow random allocation of patients to Treatment A without consideration of the form of their epilepsy. The field study showed that some patients with poorly controlled seizures know of no provocative factors, and that some have absolutely no warning of an attack. All treatment aspects have one essential feature in common; they encourage the patient to have a sense of self control over his seizures. They cease to be 'something which happens to me', and become 'something which I do'. Treatment A, if seen in this

light, can be evaluated as a discrete treatment. If effective, then evaluation of the component parts can be carried out.

Treatment B: Alleviation of Psychological Disorder.

This treatment required a detailed account of the psychological and practical problems in the patient's life at the time of interview. The preliminary study showed the high incidence of symptoms of anxiety and depression. It was also observed that problems generally fell into three categories. Firstly anxiety about leaving a safe place or being in company, secondly depression due to loss of social functioning, and thirdly stress within the family as a result of disagreement about how much independence the patient should have.

Anxiety.

In the case of phobic-like anxiety, Treatment B sessions were used to give advice about anxiety management through graded exposure. This was appropriate in 27 of the 40 patients who were given Treatment B. All these patients were fearful about the probability of having a seizure in a public place, and they had a history of avoidance of specific places where they had had a seizure in the past. In all cases there was a tendency to over-rate greatly the

probability of having a seizure, and evidence that the fear of one place had generalised to include other similar places. There was a wide range in degree of disability caused by this phenomenon, varying from being completely housebound to needing to be accompanied in certain places only, such as supermarkets and buses.

It was pointed out to patients that they were overestimating the probability of having a seizure. All patients agreed that they were probably more handicapped than they needed to be as a result of their epilepsy. All patients agreed that even if they did have a seizure in a public place the consequences were not so dangerous or so unpleasant as to make it not worth attempting to overcome their fear. Although there was no discussion of any aspect of the patient's epilepsy in this treatment, targets were based on what would be reasonable and safe for that patient to achieve.

Treatment was based on four steps in all cases.

i) Identification of panic symptoms and explanations about the physiological and psychological nature of anxiety.

ii) Construction of a hierarchy graded from the least feared situation to the most feared.

iii) Setting of targets so that exposure to each of the feared situations should take place and progress be

maintained up the hierarchy.

iv) Evaluation of progress and repetition of previous explanations and instructions were given at each session after the first.

Depression

All 40 patients given Treatment B complained of at least some symptoms of depression, such as tearfulness and feeling that life was not worth living. Some patients had some biological symptoms, such as sleep and appetite disturbance. No patient was severely clinically depressed at the time of initial assessment. The main cause identified for feelings of worthlessness, helplessness and sadness was loss of some aspect of social functioning. In many cases this was secondary to the kind of anxiety problem described above. In other cases it was due to job loss or loss of some activity such as driving. Many people felt that they were totally isolated by their epilepsy.

Treatment was based on 3 steps in all cases.

i) Re-evaluating permanently lost functions to make them appear less important.

ii) Re-assessing the probability of regaining some functions.

iii) Finding new sources of reinforcement. Information was given about Employment Rehabilitation Centres and the Epilepsy Association of Scotland (In the latter case patients were deterred from making contact until the end of the treatment study. The E.A.S gives information which duplicates that used in Treatment A. and which would interfere with treatment evaluation.)

"Contract" Therapy

Parents or spouses of patients were interviewed as part of assessment procedure unless the patient lived alone. Disagreement about the management of the patient's problems and disabilities was very common. It is possible to categorise this disagreement in two directions; one where the patient felt that he should more independent and that he was over-protected and "suffocated", and the other where the relative felt that the patient was too dependent and inactive. Treatment was based on simple contract therapy aimed at increasing the level of patient/relative agreement and communication.
There were 3 steps.

i) The relative and patient independently and with the help of the therapist made a list of activities which the patient should perform independently, activities with which he required supervision or help and activities which

he should not do at all. An example of a typical pair of lists is given in the appendix.

ii) The two lists were compared and bargaining undertaken under the guidance of the therapist to obtain reconciliation on as many points as possible. This resulted in a 'contract' containing a list of agreed activities and the circumstances under which they should be performed. (see appendix B for example) Both parties were advised not to discuss or argue over the remaining irreconcilable points.

iii) In each subsequent session both parties were congratulated on those aspects of the contract that they had been able to keep and further discussion and advice given about the remainder.

It will be observed that Treatment B, like Treatment A, has multiple elements. It is not, as might appear, three separate treatments because the majority of patients required two or more of the above procedures. They were administered concurrently so that each patient had the same amount of therapist time. It would be theoretically possible to construct three groups of patients each requiring only one of the above sub-treatments. This would require a much larger sample, because it is rare to find a patient whose psychological problems are sufficiently

clear-cut for one and one only of the above to be appropriate. Since it is rare there would not be much advantage in evaluating each procedure separately. The point here is to provide a general procedure which will cover almost all problems and with a central common feature of identifying the cause or causes of psychological distress and applying a problem solving approach to it.

3. PATIENT SELECTION.

It has already been stated that the target population for this study is patients with epilepsy attending specialist out-patient clinics. Since the aim is to evaluate treatments with a potentially wide application then patient selection criteria should be kept as minimal as possible. The following were considered the minimum possible to make the study practicable and to avoid confounding effects.

Methodological Considerations.

There must be evidence that seizure frequency is relatively constant so that 'improvement' can not be accounted for solely in terms of natural fluctuation.

There can be no change in drug treatment during any stage of baseline or treatment. Drug or drug dosage changes during follow-up may be tolerated provided that there is no change in seizure frequency for three weeks subsequent to the change. Patients whose seizure frequency changes during follow-up, after manipulation of anticonvulsant drugs must either be excluded, or data used only up until the time of that manipulation.

Practical Considerations.

Patients must agree that their seizure control is poor. If they are happy with their degree of control then treatment which relies on self-motivation is not a practical option.

Patients must have at least two seizures per week at the start of treatment otherwise the follow-up period required to evaluate treatment effect would need to be impracticably long.

Patients must have adequate cognitive ability to benefit from the treatments in question. They must be able to express themselves well enough for the therapist to gather the necessary information and they must be able to comprehend instructions. It is essential that they should be able to keep accurate records of seizure frequency.

Patients should be complying with drug therapy before and during the study. Frequent serum concentration monitoring during the study is not a practical option, but anticonvulsant blood levels should be shown to be within the therapeutic range before baseline.

4. EXPERIMENTAL DESIGN

There are two possible experimental designs which can be used to evaluate treatment effects. In one, subjects are allocated randomly to either a treatment condition or to a 'control' condition for a period of time. At the end of this time the two groups are compared. In the case of the alternative design, there is a baseline phase, a treatment phase and a follow-up phase, each with sufficient observation points for statistical analysis, and pre- and post- treatment comparisons are made. In the first a 'between subjects' comparison is made, and in the second a 'within subjects' comparison is made. The second type of design has five distinct advantages over the first.

i) It eliminates the between subjects variance caused by having two independent samples, one for a control group and one for a treatment group. If the samples are matched, then such variance is minimised, but a 'within subjects' design ensures that there is no error due to individual

differences because the 'control' group becomes the treatment group after baseline.

ii) A baseline must be long enough to ensure that it is stationary but it does not have to be as long as the treatment part of the experiment. Data from a control group would have to be collected over a period as long as treatment. By shortening the length of time during which control information is collected, error variance due to chance interventions is reduced.

iii) A "no treatment" control group in this study would have to keep an accurate weekly seizure record for the same length of time as the treatment and follow-up phases were taking place in the other group (i.e. 36 weeks). A proportion would certainly fail to do this unless frequent encouragement was given. If a proportion "drops out" of the control group not only would more subjects be required, but also results become rather difficult to interpret. If, on the other hand, frequent encouragement to keep records is given, the "no treatment" group becomes much less a "no treatment" group than treated patients during baseline.

iv) It would be very difficult to ask a psychologically distressed patient with poor seizure control to co-operate with an experiment for 36 weeks without offering any treatment. It would be impossible to ask such a patient

not to seek any other kind of psychological counselling from G.Ps, social workers or other agency during that period. Many treatment studies use a "waiting list" control group to overcome this problem. In order to ensure that enough patients have enough seizures to make treatment evaluation possible, this study will have to run for several months. Several months is too long for a waiting list in this group of patients.

v) Using the same patients as a baseline "control" group and then as a treatment group is very economical in terms of numbers of subjects required.
Treatments should be totally independent of each other. They should be administered either to two independent matched samples or to the same sample over two separate time periods. Normally, in the latter case, a wash-out period would be allowed, but these treatments are educational and cannot be unlearned.

It was decided to adopt a 'within subjects' design, bearing in mind the following points in determining its precise form.

i) It is intended that the overall effectivenes should be measured, and that the relative effectiveness of each treatment should be compared.

ii) Any subject with significant psychological disorder

could in theory benefit from both treatments. Therefore the combined effectiveness should be evaluated.

iii) Subjects without significant psychological disorder cannot benefit from Treatment B.

Figure 2. shows the experimental design which, in the view of the author, is the most economical in terms of size of sample and therapist time, the most productive in terms of information gained; and which obeys all the above principles. In essence it is a cross-over design. Patients will be selected consecutively from the parent population and those with psychological disorder randomly allocated to Group 2 or 3.

5. OUTCOME MEASURES

i) Seizure Variables

WSR. The primary purpose of this treatment experiment is to measure the effect of certain psychological treatments on seizure frequency. The main dependent variable, therefore, is weekly seizure rate (WSR). Subjects were given daily diary forms and filled in the times at which their seizures occurred. The forms were collected at each visit and a weekly count made.

Seizure Duration. Patients' relatives were asked to record seizure duration, but this proved too inaccurate for use as an outcome measure. Most relatives simply estimated time and frequently there was disagreement between two observers. In many cases the exact beginning and end of seizures could not be determined due to 'auras' or periods of post-ictal confusion. It would be impossible for patients with no relatives to record seizure duration.

Control Ratings. Patients were asked to rate the control of their epilepsy on a three point scale, as in the field study. Only patients who rated their control as poor were included in the treatment study. Control ratings were also used as an outcome measure. At the end of follow-up patients were asked to rate control of their epilepsy on the same three point scale. In the field study neurologists rated seizure control on the same scale. Neurologists' ratings were not used as an outcome measure because it was assumed that their rating would be based simply on seizure frequency and patient's degree of satisfaction with control. Both these factors are measured (i and ii) and so no additional information would be obtained.

ii) Psychological Variables.

In previous chapters it has been noted that there is more to the management of epilepsy than seizure control. Psychological disturbance is common in epilepsy and may require treatment in its own right. This study cannot be complete without some measurement of the effect of intervention on psychological state.

It has also been noted, both in the literature review and in the field study, that anxiety and depression are the most commonly reported psychological complaints. Some objective measure of anxiety and depression symptom constellations is necessary. Degree of psychological disorder must be assessed before treatment in order to decide to which treatment condition patients should be assigned: patients with no measurable psychological disorder cannot be given Treatment B. It is also important to assess degree of psychological disorder post treatment. The theoretical basis for selecting Treatment B was to see what effect alleviating psychological pathology has on seizure frequency. Change in psychological pathology must, therefore, be measured as well as change in seizure frequency.

GHQ This questionnaire provides quickly and cheaply a single measure of non-psychotic psychological distress. It was selected because it has been shown to be a reliable research tool for separating groups into 'case' and

'non-case'. Subjects scoring above a cut-off point are deemed to have significant psychological disorder (42). This is exactly what is required in this study to determine whether or not patients should receive Treatment B. The questionnaire was also used as an outcome measure to provide a single measure of post-treatment psychological disturbance. The GHQ 60 was rejected because despite its length (60 items) it has negligible advantages over the thirty item version the GHQ 30. The GHQ 28 allows distinction between various types of disorder, but since anxiety and depression measures were to be used in any case, this is not an advantage.

Goldberg (42) recommends 4/5 as a threshold score for "just significant clinical disturbance."

STAI The State-Trait Anxiety Inventory was devised by Spielberger, Gorsuch and Lushene, and extensive reliability studies have been carried out (144). The scale provides two measures of anxiety; 'State' anxiety is assessed in terms of score on a 20 item questionnaire concerned with the patient's feelings at the time of completing it; 'Trait' anxiety is assessed by means of a similar questionnaire, except that in this case the patient is asked to record how he generally feels. Both questionnaires are easily intelligible and can be completed quickly. Many anxiety schedules contain items concerning the physiological manifestations of anxiety,

such as dizziness, palpitations and tingling. In this sample such items could be confounded with sensations associated with seizures. The STAI contains no such items. The advantage of using a scale which distinguishes between trait and state anxiety is that treatment effect can be measured more precisely. Trait anxiety, which is in a sense a personality measure, would be expected to remain relatively stable, while state anxiety would be expected to change with treatment. The trait anxiety scale therefore serves as a control against which treatment effect can be measured.

Spielberger (144) has derived college student norms for the STAI; the 50th percentile score is 39 for 'state' anxiety and 38 for 'trait' anxiety. He also gives normal data for psychiatric patients; the 50th percentile score for this group is 48 for 'state' anxiety and 47 for 'trait' anxiety.

ZUNG There are a number of self administered depression inventories available, all widely used and all with many documented reliability and validity studies. The most popular research tools appear to be the Hamilton rating scale (145), Beck's depression inventory (146), and the Zung self rating scale (147). In reviewing these scales Carroll (148) points out that the Hamilton scale is largely concerned with behavioural and somatic manifestations of depression, the Beck's scale is more

concerned with psychological and cognitive features, but the Zung scale contains a broad sample of features. The inclusion of somatic items may be a disadvantage for this study since, for example, excessive tiredness may be a symptom of depression and drug toxicity. However Gabrys and Peters (149) show the discriminative reliability of the Zung compared to other scales in separating pathologically negative attitude from realistic response to difficulties. This is an important distinction in a population of patients facing overwhelming difficulties as a result of their epilepsy, where the aim is to measure depression independently from healthy response to such difficulties.

Zung (147) compared a group of depressed patients with a normal control group on his scale. The mean score for the control group was 26 and for the depressed group before treatment was 62.

ACTIVITIES In addition to scales rating affect or degree of psychological disturbance it is necessary to obtain some measure of the functional and behavioural effect of epilepsy and the associated disorders on life style. An independent sample (N = 20), from the same parent population as the field study was asked to list activities that they would like be able to carry out but felt unable to as a direct result of their epilepsy. The nine most commonly mentioned activities were presented to the

experimental subjects and they were asked to tick the ones which they felt restricted in or barred from. Although the resultant 'score' must be interpreted with caution since the scale is not an interval scale, it does provide some indication as to degree of effect on life-style of the disorder. It also provides a valuable outcome measure since it gives an indication of the extent to which behaviour and/or attitude changes as a result of psychological intervention.

INDEPENDENCE Patients were categorised as 'independent' if they did not require assistance during or after their seizures, and if they kept their own seizure frequency records. An assessment of independence was considered necessary for two reasons. Firstly it is necessary to identify patients who are dependent on relatives to the extent where treatment would be impossible without involving them. Secondly increased independence may be a consequence of successful treatment, and as in the case of the 'Activities' scale it provides an indication of behaviour or attitude change as a result of treatment.

These measures and scales, together with the standardised instructions for patients entering the study, and the list of questions collecting demographic information, are given in Appendix C.

6. PROCEDURE

Assessment

Patients attending out-patient neurology clinics in two geographical areas of Glasgow were assessed with a view to including them in the treatment study. The days on which patient selection was made were randomly determined and on those days consecutive patients with a diagnosis of epilepsy were interviewed. The diagnosis, as in the Field Study, was made by a consultant neurologist and was based on EEG and clinical evidence. The patient was asked to rate seizure control as 'inadequate'; 'inadequate but has improved in the last two months'; or 'adequate.' All patients who rated their seizure control as 'inadequate' completed the GHQ 30, the Zung Depression Inventory, the STAI, the 'Activities' check list, the 'Independence' rating, and the Seizure questionnaire. (see Appendix C).

Records were obtained from the patient, the case file, and if possible a relative, of seizure frequency over the previous two to three months. Some patients did not have written records but were able to assert with assurance that they knew their weekly seizure rate. Patients without written records, and with no relative who was able to keep an account of seizure frequency, and who were uncertain of the frequency were excluded. In this population such cases were rare (about 2%). Most patients had some kind of

record going back to their last clinic visit. Some had records which had been immaculately kept for many years.

After this assessment procedure patients were admitted to the study if they met the criteria described in the section headed "Patient Selection".i.e.

i) They had rated their seizure control as 'inadequate'.

ii) They had had an average of at least two seizures per week for at least the last two months.

iii) They were able to complete the questionnaires and rating scales without undue help. (It was assumend that if they were able to do this then they did not have cognitive deficits severe enough to prevent them from benefiting from treatment).

Treatment

All patients whose score was 5 or above on the GHQ were randomly assigned to Groups 2 or 3. Those whose score was less than 5 were assigned to Group 1. (see Figure 2). After this procedure Group 1 had 26 subjects, Group 2 had 22 subjects and Group 3 had 23 subjects.

The experimental design was then followed as in Figure 2.

Further exclusions were made according to the criteria previously described:

i) Patients whose seizure frequency appeared to be decreasing during the six week baseline.

ii) Patients whose anticonvulsant medication was altered during baseline or treatment. If medication was altered during the follow-up phase patients were only excluded if an alteration in weekly seizure rate (WSR) - in either direction - occurred during the three weeks after the change in medication.

Final groups for data analysis were as follows:

Group 1. 19 subjects

Group 2. 21 subjects

Group 3. 19 subjects

Basic descriptors of the sample are given in Table 5.

Table 5.

Demographic Characteristics of Treatment Study Sample.

	Group 1	Group 2	Group 3
Age	27.9 13.0	32.8 12.1	34.4 11.1
Sex	8m 11f	9m 12f	8m 11f
Marital Status	4m 15s	10m 11s	10m 9s
Yrs. Since Diagnosis	15.4 10.4	20.3 13.3	17.9 11.1
Seizure Type	10 Partial 7 Mixed 2 Unknown	8 Partial 11 Mixed 2 Unknown	8 Partial 11 Mixed

Evaluation of Outcome

A record of WSR was kept throughout the 42 weeks of the trial. The rating scales and questionnaires providing the other outcome measures described in the previous section were re-administered at the end of the follow-up period.

CHAPTER 6

TREATMENT STUDY: EVALUATION OF TREATMENT EFFECTS.

1. OVERALL TREATMENT EFFECT

2. GROUP DIFFERENCES

3. TREATMENT DIFFERENCES

4. OTHER OUTCOME MEASURES

In data analysis it is useful to begin with the least sophisticated method, to consider the implications of the results and then to progress systematically to more sophisticated methods, posing questions about the meaning of the data and answering them at each stage. All this can be done within the framework of the hypotheses which form the basis of the study. Results and discussion follow this plan in each of the subsequent sections.

1. OVERALL TREATMENT EFFECT.

A. IS THERE ANY IMPROVEMENT IN SEIZURE FREQUENCY?

The first question which must be addressed is whether or not there is any evidence that psychological intervention has an effect on weekly seizure rate (WSR). The simplest way to do this is to see if WSR is lower at the end of treatment than it is at the beginning.

Figure 3. shows mean WSR in each of the 42 weeks of the study, for each of the three groups. There appears to be a generally downward trend. This is a rather inconvenient way of examining the data because of the large number of data points and the variance between them causing a zig-zagging effect.

Figure 4. summarises Figure 3. by plotting mean WSR at the beginning and end of baseline, first treatment, second treatment, and follow up. It appears that WSR has fallen during the time periods where treatment was administered. WSR at the end of follow-up appears to be lower than during baseline. The simplest test to see if mean WSR at the end of the study is lower than at the beginning is a paired sample t - test. The assumptions required for the

use of this test are met.(150). These are firstly that the responses (in this case WSR) should constitute random samples from the distribution of all such responses, secondly that they are taken from a normal distribution and thirdly that the variance of both sets of responses is equivalent. Normality of distribution of mean WSR in each of the time periods can be assumed - the degree of skewness is acceptable in a sample of this size.

A paired sample t - test comparing baseline mean WSR with mean WSR for the second follow-up period shows a highly significant difference.

$$t = 6.27 \quad p < 0.001$$

However until it has been established that improvement occurred during treatment, and only during treatment, it may not be concluded that the improvement is a result of treatment. Further analysis to this end is carried out in sub-sections B and C.

Another way of presenting overall treatment effect is illustrated in Figure 5. WSR change scores are obtained by the following operation: Mean Baseline WSR - Mean last six weeks Follow up WSR/ Mean Baseline WSR X 100. A frequency plot of numbers of patients against percent change in WSR is shown. Final WSRs and Control ratings are plotted on

the same figure but these aspects are discussed in section 4. of this chapter. It will be seen that about 50% of the sample improve by 50%.

B. WHEN DOES IMPROVEMENT BEGIN?

Firstly it is necessary to rule out the possibility that patients had begun to improve before treatment began. If this was the case then the decrease could simply be a continuation of a pre-treatment trend.

The fact of being included in an experimental trial, the assessment procedure and the encouragement to keep a daily seizure record might, separately or in combination, have caused a reduction in WSR before the treatment phases began. Demonstrating a stable baseline not only proves that patients had not in general begun to improve before treatment but also indicates that improvement was not simply attributable to a placebo effect.

Figure 3. shows mean WSR for each of the six weeks of the baseline for each of the three treatment groups. It is necessary to establish that baseline was stable for each of the three groups independently because at a later stage treatment outcome will be evaluated separately in each of the three groups. Each must have a stable baseline before any conclusions about treatment effect may be drawn.

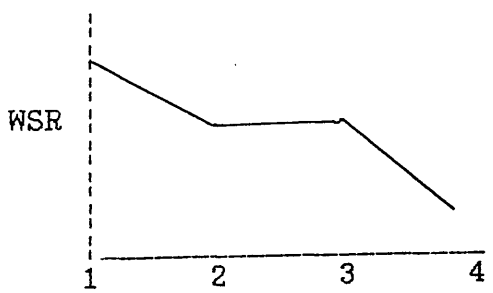
Oneway analysis of variance allows comparison of mean seizure frequency for week one with mean seizure frequency for week six; that is from the beginning to the end of baseline. The Statistical Package for Social Sciences X version of this test, {SPSSX (151)} also allows comparisons of ranges and gives tests of homogeneity of variance. Results showed no differences between means, ranges or variance between beginning and end of baseline for any of the three treatment groups. It was concluded that the six week baseline period was stable for each of the three groups.

It might be remotely possible that improvement follows a step-wise course so that although baseline is stable it was preceded by a higher WSR and will be succeeded by a lower WSR irrespective of treatment. The diagram shows this theoretical pattern.

1-2 Pre-baseline

2-3 Baseline

3-4 Post-baseline



It was considered that a baseline of six weeks was long enough to make this extremely unlikely.

As a further safeguard patient records during the two months prior to the start of baseline were examined. It will be recalled that patients were not accepted for the study unless they had such records showing an average WSR of at least two during this period and showing no pre baseline downward trend.

It was concluded that the six week baseline period was representative of the previous two month pre-intervention period.

C. WHEN DOES IMPROVEMENT END?

Another possibility which must be considered is that once improvement began it continued in a linear fashion during the follow-up periods and possibly beyond them. Further paired sample t - tests would allow some conclusions to be drawn about the course of improvement but simply comparing pairs of means for each of the phases has drawbacks. These have been itemised by Norusis (151) Firstly each t - test would not be independent because the same means would be used in overlapping combinations. There is consequently a risk of type 1 error; that is calling too many differences significant. Secondly a single test of the hypothesis that there is no change over the whole period of investigation

would not be available.

The best available statistical tool for examining changes over time, with particular reference to change in slope following an intervention, is time series analysis. This technique would allow:

i) the use of all 42 observation points.

ii) naturally occurring cyclical changes in seizure frequency to be "ironed out" of the data, and measurement of any residual overall change.

iii) comparison of the slope during treatment with the slope during follow-up.

iv) investigation of trends towards continued improvement or relapse during follow-up.

v) comparison of the change in slope occurring after treatment A. with the change in slope occurring after treatment B.

The Box-Jenkins approach is the most commonly used time series model (153), but this requires at least fifty and preferably one hundred observations. This study has only 42 observation points. Follow-up could have been continued for long enough to make up the required number of observation points, but for reasons which will become

apparent this would not have been useful. Simonton's approach is more suitable to the present design (154). It requires a minimum of 5 observations on at least 20 cases. It is essentially a generalised least squares regression analysis and allows measurement of the effect of an intervention on the time series. Unfortunately the data fail to meet one of the criteria for the use of this method. It must be assumed that all within-case errors follow a first-order autoregressive scheme. In these data too many observations are too close to zero and to each other for this to be true.

The next best appropriate statistical tool is repeated measures analysis of variance. It will:

i) allow a test of the hypothesis that change in WSR continues through follow-up.

ii) allow a test of linearity of change.

iii) It overcomes the problems inherent in simply doing multiple univariate tests.

Unfortunately it will not make as efficient use of the data as time series analysis, and so the use of additional methods will be required to test all the relevant hypotheses.

Repeated measures analysis of variance was carried out using MANOVA from the Statistical Package for Social Sciences X version (151).

MANOVA allows a single test of the hypothesis that there is no overall change in WSR. It has already been seen that a t-test comparing mean baseline WSR with mean follow-up WSR is significant, and so unless there is a massive zig-zagging effect between baseline and follow-up the inclusion of intermediate mean WSRs should not make much difference. As predicted the 'F' value is highly significant and so the null hypothesis may be rejected with confidence.

$$F \text{ (d.f. } 5, 58) = 88.91 \quad p < 0.001$$

The next step is to test the null hypothesis that differences in mean WSR between successive pairs of time periods is 0. In this way a picture can be formed of where changes occurred.

Let 'Change 1' be the difference in mean WSR between Baseline and the first treatment phase, 'Change 2' the difference betwen the first and second treatment phases, 'Change 3' between second treatment and immediate

post-treatment six week period, 'Change 4' between immediate post-treatment six week period and first follow -up six weeks and 'Change 5' difference between first and second follow-up period.

Baseline Treatment 1 Treatment 2 Post-Treatment Change 1 Change 2 Change 3 Change 4

Follow-up 1 Follow-up 2 Change 5.

Table 6 shows the F values and results of univariate significance tests for each of the 'Change' variables.

Table 6.

F values and Significance levels for Differences between WSR between each of Six Six Week Periods.

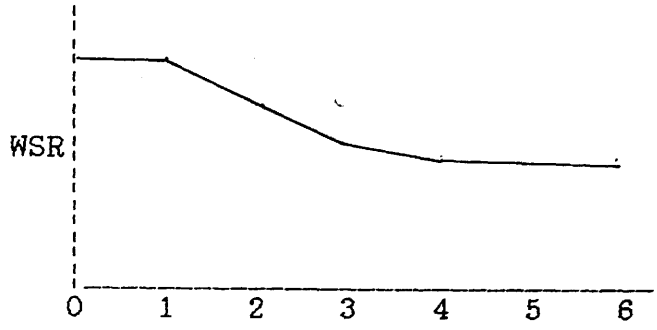
	F- Value (d.f 1, 56)	Significance
Change 1	32.18	<0.000
Change 2	39.90	<0.000
Change 3	21.70	<0.000
Change 4	3.01	0.082
Change 5	2.28	0.136

A significant change occurred between each time period except between the immediate post-treatment period and the two follow-up periods. It should be noted that the observed significance levels for individual values are not adjusted for the fact that several comparisons are being made. Strictly the assumptions needed for the use of multiple univariate tests are not met. These require that the variances of transformed variables are equal and that their covariances are 0. Bartlett's test of sphericity is significant, showing that this is not the case. The univariate tests do, however, serve as guides to the most important changes. MANOVA also carries out multivariate tests of significance. Pillais', Hotelling's, Wilk's and Roy's tests were all significant.

$$F = 10.90, \quad p < 0.000$$

MANOVA can be used to provide further information about the shape of change in WSR. To test the hypothesis that fall in mean WSR is linear across the time periods where change occurs orthogonal polynomial contrasts can be used. Results show that there is a linear fall over the two treatment phases, but that it ceases to be linear after them. An idealised graph of change in WSR, based on this information is presented in the diagram.

0-1 Baseline
1-2 Treatment 1.
2-3 Treatment 2.
3-4 Post-treatment.
4-5 Follow-up 1.
5-6 Follow-up 2.



It is concluded that most of the change in WSR occurred during the treatment phases of the experiment, that change continued through the immediate post- treatment period but did not continue through follow-up.

The fact that change in WSR levels off during follow-up so that there is no significant further change is justification for not continuing follow-up for a longer period. Given that this population has a chronic problem unsuccessfully controlled, in some cases for many years, it must be realistically expected that there will be some relapse eventually. Annual follow-up for some years is desirable to identify and possibly to counter relapse factors, but that is not within the scope of this study.

2. GROUP DIFFERENCES.

Groups 2 and 3 are random samples from the same population of patients with significant psychopathology. Group 1 is a sample from a different population: those that have no significant psychological disorder. Results of analysis of variance show that there is no difference between the groups at the start of treatment in terms of age or years since diagnosis. Chi-squared tests show no difference between them in sex, marital status, independence, type of epilepsy, and whether or not they claimed to have warnings of seizures or to know of factors triggering seizures. Analysis of variance showed no significant differences between Groups 2 and 3 in terms of the measures of psychopathology.

Any hypotheses about differences in treatment response between the groups will depend on how important we consider psychopathology to be in maintaining a high seizure frequency. If it is a very significant factor then the following hypotheses would be generated:

i) Group 1 will have a significantly lower baseline WSR than Groups 2 and 3.

ii) Groups 2 and 3 will have a larger decrease in WSR overall. (This follows because if psychological disorder is a factor causing a large proportion of patients' seizures then alleviating it will remove that large proportion, assuming for the moment that it is

alleviated).

If psychopathology is totally unimportant in maintaining seizure frequency, then no difference in treatment outcome, measured in terms of WSR, would be expected.

Evidence from the preliminary study suggests that psychopathological factors are neither very significant nor completely insignificant. It has been shown that there is a significant correlation between GHQ and seizure frequency (Pearson's r = 0.343 in the preliminary study), but it has been noted that a causal relationship in either direction cannot be inferred with any degree of certainty. Even if it is assumed that the factors underlying GHQ cause seizures, they would have to be eliminated completely to bring about a modest (around 11%) reduction in frequency.

Figure 4. shows mean WSR at the beginning and end of each phase for each of the three Groups. It will be observed that the pattern of change for groups 2 and 3 is similar, but that group 1 follows a slightly different pattern. The next logical step is to apply statistical methods to specify more precisely any differences.

A. IS THERE A DIFFERENCE IN BASELINE WSR BETWEEN THE GROUPS?

A. IS THERE A DIFFERENCE IN BASELINE WSR BETWEEN THE GROUPS?

Oneway analysis of variance was used to measure the significance of differences between the groups at baseline. Group 1 does have a lower baseline WSR, but the F ratio does not approach significance.

$$F \text{ (d.f. } 2,56) = 0.616 \quad p = 0.544$$

Neither were there significant differences between the ranges or variances of the three groups.

Thus hypothesis i) remains unsupported; it would appear from these data that psychological disorder is not related to increased seizure frequency. This finding is contrary to expectation given the significance of the correlation between GHQ and WSR, and although the small size of that correlation may account in part for these seemingly diverse findings there is a better explanation. When the procedure for patient selection is recalled, it becomes apparent that comparison of baseline WSR between Group 1 and Groups 2 and 3 is not a good experiment to test the hypothesis that WSR is related to GHQ score. Patients were only selected for Group 1 if their seizure frequency was in excess of two per week and if their GHQ score was 5 or less. The probability of finding such a patient in the parent population was about half the probability of finding a patient for Groups 2 or 3. Thus in testing hypothesis i) all patients with a seizure frequency of

less than two per week and who are rated as well controlled are omitted. It is not surprising, therefore, that the result is not significant. Examination of the correlation between WSR and GHQ in the parent population is a much better method of examining the relationship.

B. IS THERE AN OVERALL DIFFERENCE IN TREATMENT EFFECT BETWEEN THE GROUPS?

Multivariate analysis of variance (MANOVA) was repeated using the three treatment groups as a factor. There was no significant group effect on baseline to follow-up change in WSR. Thus in terms of overall treatment response each group did as well as the other two groups.

At first sight these findings appear to provide firm support for the general hypothesis that psychological disorder, measured in terms of GHQ, is not important in determining treatment outcome, and by implication is not important in maintaining seizure frequency. It must be remembered, however, that Group 1 had only one treatment and therefore half the number of treatment sessions. Thus Group 1 did as well with one treatment as Groups 2 and 3 did with two. In one sense Group 1 was more successful.

C. IS THERE A DIFFERENCE BETWEEN THE GROUPS AT ANY STAGE OF TREATMENT OR FOLLOW-UP?

Examination of Figures 3 and 4 shows that the pattern of improvement is slightly different for each of the groups. MANOVA allows the significance of these differences to be tested at each phase of treatment. Table 7 shows results in the same form as in Table 6, but in this case the group by WSR change interaction is being tested.

Table 7.

F Values and Significance Levels for Group Effect on WSR Change Between each of Six Six Week Periods.

	F- Value (d.f 1, 56)	Significance
Change 1	0.39	0.674
Change 2	4.01	0.023*
Change 3	0.86	0.425
Change 4	1.18	0.318
Change 5	0.08	0.918

Results show that there is a significant difference between the Groups after one treatment, but not at any other time.

Examination of Figure 4 shows that this difference is caused by Group 1 which appears to have greater change in WSR during the first treatment phase. During follow-up this difference evens out. Either of the models described below could explain why Group 1 appear to have done better after one treatment.

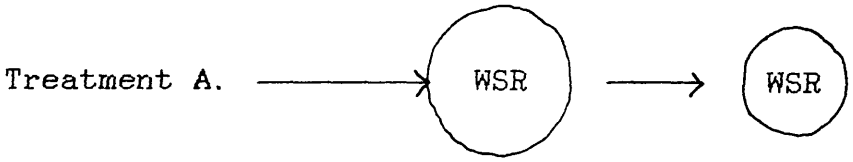
What is less clear is why the difference is not maintained. The most probable explanation is the number of treatment sessions. Group 1 has fewer; possibly if it had had more the difference would have been maintained.

D. TWO MODELS WHICH COULD EXPLAIN WHY GROUP 1 DOES AS WELL WITH ONE TREATMENT AS GROUPS 2 AND 3 DO WITH TWO.

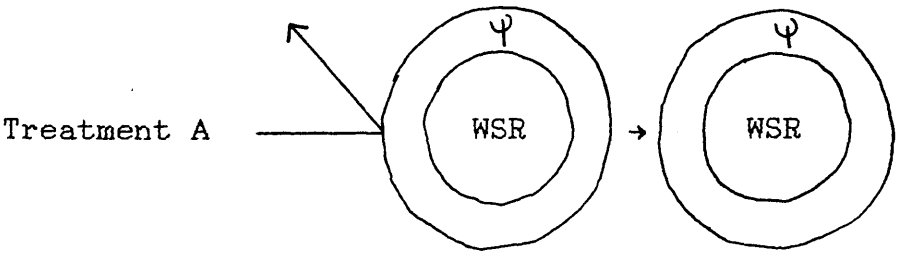
i) This result is in keeping with what is known about treatment response in general. It is generally accepted that patients with significant anxiety or depression tend to respond less well to a variety of medical and surgical treatments and that excessive anxiety interferes with learning. If we conclude that the total response of Groups 2 and 3 is only as good as Group 1 when their psychopathology has been treated then a new treatment mechanism could be suggested to fit the results so far. So far the model under consideration has been:

↑GHQ ⟶ ↑WSR and ↓GHQ ⟶ ↓WSR.

Let us suppose that psychopathology does not directly maintain a high seizure frequency but prevents patients benefiting maximally from Treatment A.
If this was so then in Group 1. Treatment A acts directly:



but in Groups 2 and 3 psychopathology (Ψ) interferes:



Treatment B might work by reducing psychopathology so that A can be effective. At this stage we have very little evidence to support this model, but examination of treatment order effects and the effect of degree of psychopathology on treatment, should allow the model either to be refuted or supported further. The former is undertaken in the next section and the latter in Chapter

7.

ii) There is an alternative explanation for the relatively rapid improvement shown by Group 1 patients. If, as discussed in a previous section, seizures in any individual are caused by n factors, then elimination of any of these factors would be expected to reduce seizure frequency. In the experimental sample all groups have the same baseline seizure frequency, X. The two treatments, A and B, aim to 'eliminate' two different types of factor, An and Bn. It is assumed that because Group 1 has no significant psychopathology that Bn = 0 in their case. The total number of seizures at baseline is some function of the number of factors. For Group 1;

$$X = f(An + Cn)$$

where C represents the unknown factors. For Groups 2 and 3;

$$X = f(An + Bn + Cn).$$

It is not unreasonable to assume that the distribution of values for 'C' is the same in all three groups. If X and C have the same values in both equations then A must be smaller for Groups 2 and 3. Therefore Treatment A, even if equally effective in eliminating An in all groups, would

have a smaller effect on X in Groups 2 and 3. Again examination of differences in treatment effects will allow further evaluation of these speculations. The only conclusion that can be drawn at the end of this section is that two treatments are as effective in reducing WSR in Groups 2 and 3 as one treatment is in Group 1.

3. TREATMENT DIFFERENCES.

A. ARE TWO TREATMENTS BETTER THAN ONE?

Results presented in Table 6 and discussed in section 1. of this chapter show that there is a further significant decrease in WSR during the second treatment in both groups. However this finding does not allow the conclusion that two treatments are better than one because it is possible that there might be a continued improvement after the first treatment without the addition of a second. Evidence for the existence of a carry-over effect is discussed below. If it can be demonstrated that such an effect does not exist then it may be concluded that two treatments are better than one.

B. IS ONE TREATMENT MORE EFFECTIVE THAN THE OTHER?

Is a treatment different when it is administered first rather than second?
It has already been demonstrated that there is no difference in overall outcome between Groups 2 and 3. Administering Treatments A then B is exactly as effective as administering B then A. However the total change during A across both Groups might be different from the total change during Treatment B.

Mean % change for both groups during:

Treatment A = 29.8% S.D. 56.8

Treatment B = 22.0% S.D. 57.7

A test of the difference between these means shows no significant difference. It is concluded that there is no difference in effectiveness between Treatments A and B.

C. IS THE EFFECT OF ADMINISTERING A TREATMENT FIRST DIFFERENT FROM ADMINISTERING IT SECOND?

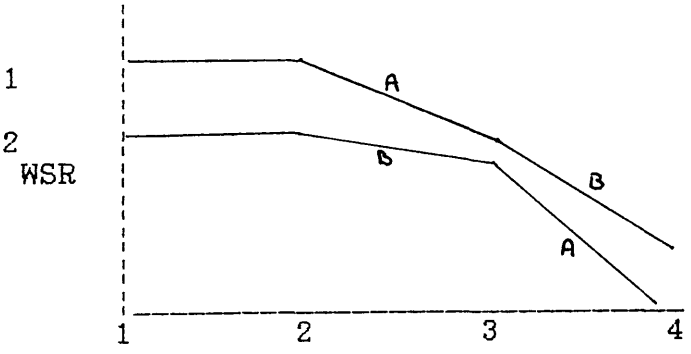
Treatments are essentially educational and cannot be withdrawn once they have been administered. There may be some carry-over effect so that a treatment continues to

cause a change in slope in WSR for some time after its final treatment session. The change in slope during the second treatment, therefore, may be caused by the summation of both treatment effects. However treatments were administered in a different order in Groups 2 and 3 and so this possibility can be investigated statistically. If there is a significant carry-over effect then it would be expected that the treatments would have a different apparent effect when they were administered second than when they were administered first; graphs representing change in WSR would tend to look like this:

1-2 Baseline

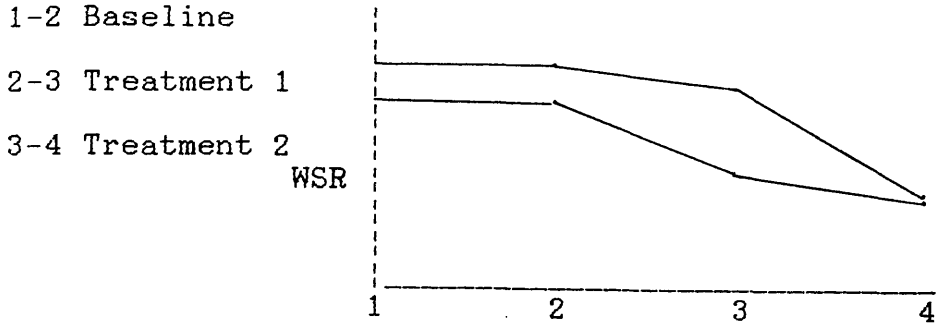
2-3 Treatment 1

3-4 Treatment 2



The carry-over effect could be measured by subtracting the effect of a treatment when it was administered first from its effect when it was administered second.

If, on the other hand, there is no significant carry-over effect then change during the treatments should be the same regardless of whether they are administered first or second.



Examination of Figure 4. shows that there is an apparent upward jump in WSR during the second treatment phase. Comparison with Figure 3 shows that this is a little misleading and is a result of the wide zig-zagging effect during that phase. Mean WSR at week 15 has been marked with an X to clarify this. If a 'best fit' line was drawn through the second treatment phase of Group 2 then the slopes during Treatments all appear rather similar regardless of whether the Treatment is A or B or whether it is administered first or second. A comparison of mean % change during A when it was administered first with mean % change when it was administered second shows no significant difference. A comparison of mean % change during B when it was administered first with mean % change when it was administered second also shows no significant difference.

These negative results suggest that there is no

significant carry-over effect thus allowing the following conclusion that it is very probable that two treatments are more effective than one treatment.

D. IMPLICATIONS OF THE RESULTS OF COMPARISONS BETWEEN TREATMENTS.

Figure 5 shows that there is a wide range of reponse to treatment. In a population with such large individual differences in treatment response it would be unwise to draw any firm conclusions about how treatment works. It is possible to make generalisations about the likely mechanism of action but even in this relatively small sample there must be a proportion of patients for whom the generalisation is not true.

In section 2., which discussed group differences, a model was proposed in which the mechanism of action of Treatment B was that it removed factors preventing subjects from benefiting from Treatment A. If this is so then Treatment A should have a much smaller effect when it is administered first than when it is administered second. It might also be expected that the combined effect of A then B is less good than B then A. Results of data analysis do not support this. In the case of the second model proposed in the previous section, there is no particular reason why order should be important. The data tend to support this

second model.

If treatments are equally effective the possibility that they are really the same treatment must be considered. Perhaps factors that the treatments had in common were more important than things which distinguished them. The checks that were made to ensure that the two treatments focused on independent aspects of the patients' condition are described in the section headed 'Procedure', but both treatments had two obvious common factors; the therapist and therapist time. If therapist time and attention is the effective ingredient then it would reasonably be expected that Group 1 would do less well since they have fewer treatment sessions. It has been demonstrated that they do not. An even more convincing argument is that treatment effect is maintained over a six month follow-up period without further therapist attention. This certainly suggests that patients have acquired some skill during treatment which is resistant to decay. An alternative hypothesis is that the common ingredient in both treatment packages is an improved sense of self-control. This might well be a result of a treatment directed at psychological disturbance, or of one directed at seizure control. An examination of the other outcome measures should give some indication of the likelihood of this hypothesis. These measures are discussed in the next section.

Another possible explanation for the similarity in effect

of both treatments could be that both brought about an improvement in drug compliance, and that this was the key component leading to treatment success. In Chapter 5 in the section dealing with subject selection it was reported that each subject's case records were examined for evidence of non-compliance and that all subjects in the study had had serum concentration of their AEDs measured and found to be at optimal levels within 3 months of the start of psychological intervention. This is a relatively crude check on compliance and it is quite possible that some patients were more consistent in taking their medication during treatment than before it. However it is extremely unlikely that this effect is large enough to account for treatment success in a significant number of cases. Although no formal assessment was made, several patients claimed that they had reduced their medication on their own initiative by the end of follow up as a result of improvement in seizure frequency. On balance it seems that changes in drug compliance could not account for the similarity in effectiveness of the two treatments and could not alter significantly the conclusions of the study.

Yet another possible explanation for the similarity in treatment effects is that both treatments simply eliminated pseudo-epileptic seizures and that the attacks left at the end of treatment are the remaining genuine epileptic seizures. The main evidence against this

possibility is the size of the treatment effect. The highest estimate of the proportion of non-epileptic seizures amongst the population of people with epilepsy is 26% (see Chapter 2 section 7.) In this sample the mean improvement in seizure frequency is nearer 50%. Fenton (90) recommends lengthy and complex treatment for pseudo-seizures and it seems unlikely that the short, simple treatments used here would be effective against them.

4. OTHER OUTCOME MEASURES.

A. IS THERE ANY EVIDENCE OF CLINICAL IMPROVEMENT OTHER THAN FALL IN WSR?

In previous sections results which show evidence of a statistically highly significant treatment effect have been presented. Statistical effects, however, are not always of much importance to the patient. If the degree of improvement is insufficient to make a difference to the patient's quality of life then the real benefits of treatment may be negligible.

The first, most simple question to be asked is whether patients' perception of seizure control changes when absolute frequency has changed. Patients were asked to rate how well their seizures were controlled on a three point scale before treatment (see Chapter 5), and only those patients who rated their control as poor were included in the study. Patients rated their seizure control on the same scale at the end of follow-up. (Patients were also asked if they felt more in control of their seizures; it will be seen that this is a quite different question and is dealt with at the end of this section.) Figure 5 shows the relationship between amount of improvement in WSR from baseline to follow up, mean WSR at

the end of follow up. It will be seen that patients who changed their control ratings from poor to good were those who improved the most.

Table 8. shows pre- and post- treatment scores on all outcome measures apart from seizure frequency. Once again paired sample t-tests are the most powerful, sensitive appropriate statistical method of comparing pre- and post-treatment means on measures which can be assumed to have a normal distribution. The 'Activities' scale is not an interval scale and is not normally distributed and so although means are quoted, a Mann-Whitney U test was carried out and the significance level refers to this result.

Table 8.

Pre- and Post- Treatment Mean Scores on Outcome Measures for each Group.

GROUP 1. n=19	Pre-Treat. Mean	Post-Treat. Mean	Significance of Comparison
GHQ	3.26	3.05	N.S.
STAI (state)	39.47	39.68	N.S.
STAI (trait)	40.00	38.68	N.S.
ZUNG	25.37	24.58	N.S.
'ACTIVITIES'	3.16	2.58	0.004

GROUP 2. n=21	Pre-Treat. Mean	Post-Treat. Mean	Significance of Comparison
GHQ	12.81	7.05	0.001
STAI (state)	59.91	50.62	0.001
STAI (trait)	53.48	48.05	0.018
ZUNG	35.67	30.05	0.001
'ACTIVITIES'	3.38	2.71	0.016

GROUP 3. n=19	Pre-Treat. Mean	Post-Treat. Mean	Significance of Comparison
GHQ	16.05	8.47	0.001
STAI (state)	62.16	53.05	0.001
STAI (trait)	56.00	51.84	0.023
ZUNG	40.32	32.74	0.001
'ACTIVITIES'	2.74	2.37	0.015

It is concluded that in terms of the measures of anxiety and depression used, Groups 2 and 3 become significantly less anxious and depressed as a result of treatment.

Group 1 was not expected to become less anxious or depressed because its scores on the rating scales were normal at the start of the experiment.

Table 8. shows that there was a significant reduction in the number of work related and social activities that patients felt restricted in or barred from as a result of their epilepsy. 'Independence' was also rated pre- and post- treatment. Eleven patients in Group 1, ten in Group 2 and eight in Group 3 were 'independent' before treatment. Fourteen patients in Group 1, twelve in Group 2 and eleven in Group 3 were 'independent' after treatment. The change in the 'Activities' scale and the small increase in number of 'independent' patients suggests that there may be a behavioural change as well as a change in symptom reporting.

It will be noted that in terms of STAI scores 'Trait' anxiety has fallen as well as 'State' anxiety. Test-retest reliability studies have been carried out for the scales (144) and show that test - retest correlation ranges from 0.73 to 0.86. for 'Trait' anxiety. Parrino (155) used the scales on a psychiatric population before

and after treatment for phobic anxiety. He found a significant reduction in 'State' anxiety, but 'Trait' anxiety remained unchanged. It appears then that contrary to expectation based on previous evidence, patients in this sample have changed their view of how anxious they generally feel. This is likely to be result of the long time period between administrations of the test. If patients have been feeling less anxious for some time then they will respond differently to the question "how do you generally feel" than if their improvement has been recent.

In addition to the standardised questionnaires patients were asked if they felt more or less in control of their seizures and psychological problems at the end of treatment that they did at the beginning. (This is a different question from asking for a rating of how well seizures are controlled, since it deals with sense of self-control and is therefore active rather than passive.) The question was apparently not very meaningful since all but two patients said that they felt more in control of their disorder. These two patients had shown an improvement in WSR of 29% and 37% respectively. Patients who showed relatively little treatment effect still reponded affirmatively. This serves to illustrate the value of standardised rating scales since they are less open to bias caused by patients wishing to give the "correct" answer.

B. IS THE CLINICAL IMPROVEMENT SUFFICIENT TO MAKE TREATMENT COST-EFFECTIVE?

Table 8 reveals that Groups 2 and 3 are drawn from a highly anxious and depressed population. Normal data for these scales are presented in the section headed 'OUTCOME MEASURES' Chapter 5. It will also be observed that at the end of the study subjects are still highly anxious and slightly depressed compared to 'normal' subjects even although there has been a significant improvement. Most are still unemployed and most still feel restricted in or barred from at least 2 activities. Only 8 subjects who were unable to cope alone with their seizures before treatment were able to cope after treatment. Despite the gains of treatment at the end of the study there are still 26 patients with a seizure frequency in excess of 2 per week and 24 patients with a GHQ score in the 'caseness' range. Nineteen patients have both these characteristics. Thus almost half the sample, in the light of the arguments in favour of psychological intervention presented in the Introduction, still require psychological intervention. There are two possible alternative explanations of this result; more treatment sessions may be required to help some patients or there may be some patients for whom these treatments are not effective.

The fact that some patients may still require treatment at the end of the study gives only an overall indication of treatment cost-effectiveness. The question of whether an individual patient's decrease in seizure frequency represents a clinically significant improvement remains open. It appears that psychopathology has been reduced and that there are some behavioural manifestations of the improvement. If the same patients are improving on all these measures then it is reasonable to conclude that treatment causes a clinically significant effect. If some patients are improving on one measure and some on another the gain, and by implication the cost-effectiveness of treatment, is less apparent. An attempt to relate patient characteristics to outcome may help to clarify this; such an attempt is made in the following chapter.

C. THE IMPLICATION FOR THE RELATIONSHIP BETWEEN WSR AND PSYCHOPATHOLOGY.

The conclusion above that anxiety and depression in Groups 2 an 3 improves with treatment does not specify which treatment. It may be that the two groups become less anxious and depressed as a direct result of Treatment B. The improvement in psychological state may also be due to the indirect effect of a reduction in seizures. It may be due simply to the effect of being included in the study. It is not possible to disentangle these alternatives with

any degree of certainty. Scores on the rating scales obtained between treatments might have been helpful, but they were not administered at this point. Enough is known about patients' response to psychological treatment in general for this lack of information to be relatively unimportant. It can safely be assumed that any new treatment, or even being placed on a waiting list, would have some effect in reducing patients' GHQ scores, etc. It can also be assumed that a treatment specifically aimed at anxiety and depression will be more effective in alleviating them than one not aimed at anxiety and depression. It can be accepted that Treatment B was an important agent, although almost certainly not the only agent, in reducing psychological symptoms. It has already been demonstrated that WSR falls during Treatment B. Taken together this evidence provides support for the hypothesis that alleviating psychological disorder can decrease seizure frequency.

It is concluded that since WSR and scores on measures of psychopathology fall during Treatment B there is in all probability a mechanism by which alleviating psychological disorder decreases seizure frequency.

The evidence that Treatment B, the treatment aimed at alleviating patients' psychological problems, succeeds in doing this and causes a reduction in WSR, has been discussed. If alleviating psychological distress brings

about a reduction in seizure frequency then it can be inferred that psychological distress can raise seizure frequency.

If it can be shown that there is a mathematically functional relationship between change in psychopathology measures and change in WSR then this provides further support for the hypothesised relationship between WSR and psychological distress, although a spurious relationship is still a logical possibility.

Table 9. shows Pearson's correlation coefficients between change in WSR and change in psychopathology measures. "Change" in both instances is pre-treatment score - post-treatment score/ pre-treatment score.

Table 9.

Correlations Between Change in Psychopathology Measures and Change in WSR.

~	GHQ (ch)	STAIS (ch)	STAIT (ch)	ZUNG (ch)
WSR (change)	.2406	.2116	.1594	.1499
p =	.067	.095	.163	.178

None of these correlations is significant, although the

correlation between WSR (ch) and GHQ (ch) approaches significance. An explanation for these negative results may be found in the nature of the treatments. The WSR (ch) variable is a measure of total change from before the first treatment until after the second. One of the treatments, Treatment A, is not concerned with psychopathology. It would not be expected, therefore, that there should be a significant relationship between change in psychopathology and change in WSR during Treatment A. If, instead of using total change over both treatments, we examine total change during Treatment A and during Treatment B separately, results may take on a different appearance.

Table 10 shows Pearson's correlations between pre - post psychopathology measures and pre - post WSR change during Treatment A and during Treatment B.

Table 10.

Correlations between change in WSR and change in psychopathology measures for Treatment A and Treatment B.

~	GHQ (ch)	STAIS (ch)	STAIT (ch)	ZUNG (ch)
T.A WSR (ch)	.1067	.0646	.0009	.1138
p =	.318	.346	.498	.242
T.B WSR (ch)	.4138	.3980	.2008	.2993
p =	.004	.005	.107	.030

It will be seen that the correlations between WSR change and psychopathology change during Treatment A are negligible while the correlations between WSR change and psychopathology change during Treatment B are significant except in the case of trait anxiety (STAIT), which it will be recalled changes the least with treatment.

These results indicate that there is a mathematically functional relationship between change in psychopathology measures and change in WSR.

The implications of this section can be summarised as follows: Treatment B has been shown to alleviate psychological distress. It is inferred that alleviating psychological distress causes a reduction in seizure

frequency, and that the amount of reduction is related to the amount of change recorded in the anxiety and depression rating scales.

CHAPTER 7.

THE CONCEPT OF SEVERITY.

1. BASELINE SEIZURE FREQUENCY

2. PRE-TREATMENT PSYCHOPATHOLOGY

3. TIME SINCE DIAGNOSIS

4. RESTRICTED ACTIVITIES

5. CONCLUSIONS AND IMPLICATIONS

Until this point results have been discussed as though variance in treatment response was unimportant. In fact there is considerable variance in treatment response; some patients have no seizures during six months of follow-up, while others have slightly more than at baseline. This chapter, and the subsequent three chapters, are concerned with variables, and groups of variables, which might explain why some patients benefit more from treatment than others.

The concept of severity has been discussed previously; it

will be recalled that it was concluded that the concept includes several factors and cannot be considered as a single entity. In a general way it may be expected that, in common with many psychological treatment studies, pre-treatment 'severity' might have an adverse effect on treatment response. If each of the components of 'severity' is examined independently, however, it will seen that such an hypothesis would be an over-simplification.

1. "SEVERITY" IN TERMS OF BASELINE SEIZURE FREQUENCY

There is no particular reason why a high baseline seizure frequency should be associated with relatively poor outcome. It might be suggested that very poor seizure control at baseline was an indication of the extent to which previous treatments had failed, but all previous treatments were pharmacological and so previous therapeutic failure is not likely to reduce the probability of present therapeutic success.

There are reasons why a high baseline seizure frequency might be associated with better treatment response. Firstly, in the case of Treatment A, the more frequent the seizures the greater the opportunity for practising and perfecting techniques of seizure interruption. Secondly, it may be that cases where pharmacological methods have

been the least effective are those cases where psychological methods will be the most effective. This might well be true, for example, in the case of a patient with a high proportion of pseudo-epileptic seizures. It might equally be true of a patient in whom psychological factors were a significant, powerful seizure potentiator.

Using a paired sample t-test, mean baseline seizure frequency for the 20 patients whose WSR decreased by 59% or more between baseline and the end of follow-up, (the best third) was compared with mean baseline seizure frequency for the 20 patients whose WSR decreased by 26% or less, (the worst third).
The result did not approach significance. In terms of these data, baseline seizure frequency appears to be irrelevant to treatment outcome. This does not exclude the possibility, however, that in some individual cases a high baseline frequency might confer an advantage, as suggested above.

2. "SEVERITY" IN TERMS OF PRE-TREATMENT SCORES ON PSYCHOPATHOLOGY SCALES.

Pre-treatment scores on the four psychopathology scales, (GHQ, STAIS, STAIT, ZUNG) are given in Table 6. Group 1 patients, by definition, have a normal GHQ score, and

insignificant levels of anxiety and depression measured in terms of the other scales. Groups 2 and 3 are significantly anxious and depressed in terms of these scales. Differences in outcome between the Groups have been discussed in Chapter 4 section b. At this point we are concerned with the effect of 'severity' of pre-treatment psychopathology on final outcome in terms of weekly seizure rate. The effect on treatment response may not be the same for both treatments; it is necessary to examine the effect on Treatment A and Treatment B separately.

A) Anxiety and depression might interfere with ability to learn the techniques presented in Treatment A. If so the more psychologically distressed patients will benefit less from Treatment A.

When treatment order effect was the topic of discussion the above hypothesis was considered. At that point in the argument it was suggested that Treatment A administered first would be less effective than Treatment A administered second. If anxiety and depression truly interfere with response to Treatment A then when these symptoms have been alleviated by Treatment B, A should have a greater probability of working. It was demonstrated that Treatment A was equally effective whether administered first or second. However, at that stage the effect of severity was not considered. The most severely

anxious and depressed patients might indeed fail to respond to Treatment A. If so, there will be an inverse relationship between pre-treatment scores on psychopathology scales and change in WSR during Treatment A.

Table 11 shows Pearson's correlation coefficients between change in WSR during both treatments {T.A WSR (ch) and T.B WSR (ch)} and pre-treatment scores on the psychopathology scale.

Table 11

Correlations between change in WSR during Treatment A and Treatment B and pre-treatment psychopathology measures.

~	GHQ	STAIS	STAIT	ZUNG
T.A WSR (ch)	.1558	.2205	.1290	.1535
p =	.168	.086	.214	.172
T.B WSR (ch)	.0603	-.0979	-.0444	-.4758*
p =	.356	.274	.393	.001*

There is no inverse relationship between change in seizure frequency during Treatment A. and pre-treatment scores on the psychopathology scales. In fact the correlations are all positive and, in the case of state anxiety, (STAIS) approaching significance. The hypothesis that anxiety and depression may interfere with Treatment A is not

confirmed. There may be a very weak trend towards the converse; that patients with higher initial levels do slightly better.

B) It might be expected that patients whose anxiety and/or depression is severe will not benefit from a treatment as short and simple as Treatment B. If Treatment B is not effective in alleviating psychological disturbance in the more chronic or complex cases then it will not be effective in reducing seizure frequency in these cases.

This hypothesis must be dealt with in two stages. The first stage is to test whether high pre-treatment psychopathology scores are a poor prognostic sign for treatment outcome in terms of reduction in psychopathology. The second stage is to test whether they are a poor prognostic sign for outcome in terms of reduction in seizure frequency.

Table 12 gives Pearson's correlations between pre-treatment measure of psychopathology (GHQ etc.) and change in measures of psychopathology {GHQ (ch) etc. } Change scores were pre-treatment score - post-treatment score/ pre-treatment score.

Table 12

Correlations between pre-treatment and change measures of psychopathology.

~	GHQ	STAIS	STAIT	ZUNG
GHQ (ch)	.7139			
STAIS (ch)		.5496		
STAIT (ch)			.5960	
ZUNG (ch)				.7337

$p < 0.0001$ in each case.

It is clear from these results that in terms of amount of change in score on these measures the higher the initial level the greater the improvement. It may be possible that those patients who began the treatment trial with the highest anxiety/depression levels were those who ended the trial with the lowest levels. In order to test this the sample was divided into two groups; 'high' scorers and 'low' scorers on each of the psychopathology measures. The two groups were then compared in terms of final score on the same measure, using paired sample t-tests. There were no significant differences; it appears that the same end point is reached whatever the initial level. In terms of outcome on the psychopathology scales initial high levels are neither a bad prognostic sign, nor a good one.

The results displayed in Table 11 show that change in WSR during Treatment B is inversely related to initial ZUNG score. It becomes clear that although overall ZUNG scores improve with treatment (see Table 8), the higher the initial score the poorer the treatment response, not in terms of change on the ZUNG scale, but in terms of improvement in seizure frequency. This finding tends to weaken the evidence for a causal relationship between depression and seizure frequency. If depressed patients do less well in terms of improvement in WSR, despite a very substantial improvement in their depression, then it is unlikely that depression is maintaining a high seizure frequency. This conclusion has important implications which are discussed at the end of this section.

Correlation, although useful as an indicator of what factors might be associated with good or poor treatment response, is rather a imprecise test. One or two isolated results outlying the rest of the data can produce a seemingly highly significant result. A further test would be to compare a group of relatively low scorers on the pre-treatment Zung scale with a group of relatively high scorers. If the correlation is truly indicative of an important effect then the low scorers will have a significantly greater treatment reponse than the high scorers. A t-test is appropriate given that Zung scores and WSR change scores may be considered to be normally distributed.

Table 13

Comparison in Outcome Between Patients Scoring above the 50th percentile and those Scoring Below on the ZUNG Depression Scale.

	Mean % Change in WSR
Pre-Treatment Zung score above 31	34
Pre-Treatment Zung score below 31	46

$t = 3.21 \quad p < 0.002$

3. "SEVERITY" IN TERMS OF TIME SINCE DIAGNOSIS.

Time since diagnosis is essentially a measure of chronicity. Experience in the use of psychological therapies would lead one to suppose that the longer a patient has had a problem, the more different clinicians he has seen, and the more different treatments he has tried the less likely he is to do well. However it must be remembered that none of these patients has had any formal psychological therapy before and so there is no particular reason to suppose that the usual rule will apply.

The variable 'Time Since Diagnosis' is not normally distributed: the range is from 0 to 30 years with a median of 3 years. Non-parametric statistics are the most appropriate in this case.

Results show a Spearman's correlation coefficient of -.23, $p = 0.04$, between change in WSR and time since diagnosis. The scattergram showed wide scatter and there was no suggestion of clusters of patients with a long history and poor outcome or short history and good outcome.

As a further test the sample was divided into two groups, those with a history of longer than 3 years and those with a history of 3 years or less. Mean baseline WSR and mean total change in WSR were compared for the two groups 'chronic' and 'not chronic'. Differences between the groups did not approach significance. It is apparent, therefore, that if chronicity is a poor prognostic sign it is a very weak one.

4. "SEVERITY" IN TERMS OF RESTRICTED ACTIVITIES.

Another possible indicator of severity is functional impact of the disorder. In this study the measure of functional impact is the number of normal activities that the patient feels restricted in or barred from as a result of his epilepsy. Patients' attitude to their disability tends to vary greatly from one individual to another. Some with a relatively low seizure frequency (for this sample) were housebound and dependent. Others refused to give up any activity; several patients in the study with a seizure frequency in excess of two per week were still driving a car on a regular basis.

The 'Activities' variable is a 9 point ordinal scale, with a pre-treatment mode score of 3. The sample was divided into two groups, those scoring above 3, (18 subjects) and those scoring below 3 (15 subjects.) A t - test showed no difference in baseline WSR or total change in WSR between the groups. Pre-treatment disability level, measured in this way, is not related to outcome.

5. CONCLUSIONS AND IMPLICATIONS.

In conclusion, only one aspect of pre-treatment 'severity' is a predictor of treatment outcome in terms of seizure frequency. An initially high score on the Zung scale appears to be associated with less reduction in seizure frequency during Treatment B., even although Treatment B appears to be effective in reducing score on the Zung scale. If depression were actively increasing seizure frequency then alleviating it should decrease seizure frequency. The fact that it does not suggests that there is no causal relationship in the direction shown below:

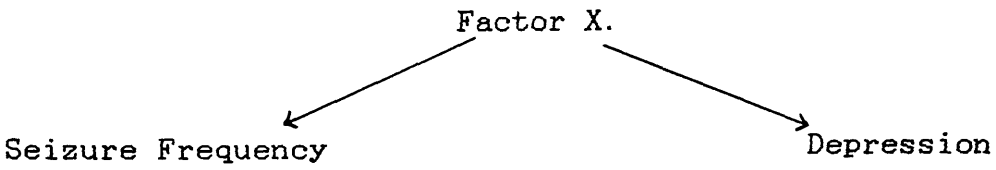
Depression ⟶ Seizure Frequency.

Neither can there be a significant causal relationship in the opposite direction:

Seizure Frequency ⟶ Depression.

If there were then it seems mOst unlikely that depression could be effectively treated while seizure frequency remained relatively unchanged.

How, then, can the relationship between pre-treatment Zung score and amount of reduction in WSR be explained? It is proposed that some unknown factor causes both depression and seizures to be resistant to the effects of psychological treatment.



This factor would be a predictor of poor treatment response and therefore of practical and theoretical importance. Variables which may by their presence, or by their absence, predict treatment response are examined in the subsequent chapter. It may be possible to show that one of these is related to both seizure frequency and to depression.

CHAPTER 8.

FACTORS POTENTIALLY ADVANTAGEOUS FOR TREATMENT.

1. AURAS

2. FACTORS WHICH PROVOKE SEIZURES

3. INDEPENDENCE

This section examines factors which might be considered advantageous for treatment. If they are then they may be predictors of treatment response, or even pre-requisites for a successful reduction in seizure frequency.

At the end of the previous section, under 'Conclusions and Implications', a question was raised concerning the relationship between seizure frequency and score on the Zung depression scale. It appears that a pre-treatment high Zung score is associated with less improvement in seizure frequency. Since Zung score falls significantly with treatment it seems unlikely that there could be a direct relationship between the two variables. Some other factor might link seizure frequency and depression and explain these results. It is proposed that the lack of one

or other of the factors discussed in this section might be related to depression and might also be related to poor treatment response. Each factor will be examined with this in view.

1. AURAS

An 'aura' is generally defined as some sensory experience or alteration in consciousness which precedes a seizure. In the case of temporal lobe seizures the aura is frequently some vivid sensory hallucination, although in other cases the feeling is indescribable. Patients who do not have temporal lobe epilepsy not infrequently experience some indication that they are about to have a seizure. Strictly the 'auras' associated with temporal lobe epilepsy are part of the seizure itself. Probably the feeling of an impending seizure in other forms of epilepsy also represents electrical changes preceding the actual burst of activity which constitutes the seizure itself. For the purpose of this discussion any kind of seizure warning will be termed an aura.

a) Auras in Relation to Treatment Response.

In this sample 42 patients experience an aura or some form of warning that they are about to have a seizure, and 17

do not. In this case the hypothesis is clear. Treatment A almost requires subjects to have sufficient notice of a seizure to carry out some form of interruption technique. It is predicted, therefore, that patients with an aura will do better during Treatment A than those without. There is no particular reason to assume that the presence of an aura will have any influence on susceptibility to Treatment B.

Table 13 shows mean % changes in WSR from baseline to final follow - up for subjects who experience an aura and those who do not. There was no significant difference in baseline seizure frequency between these two groups, and the distribution of % change in WSR was approximately normal.

Table 13

Difference in Treatment Response Between Subjects with Aura and Those Without.

Subjects with 'Aura' n = 42	Mean % change in WSR 49.77
Subjects without 'Aura' n = 17	Mean % change in WSR 16.39

t = 2.49 p = 0.02

If the above hypothesis holds it would be expected that almost all this difference between the two groups occurs

during Treatment A. A comparison between change during treatment A and change during Treatment B can only be made for Groups 2 and 3 (n = 40). Within these groups there are only 9 subjects who do not experience an aura. This sets limits on statistical analysis and probably explains why mean change during Treatment A during Treatment B shows no significant difference between patients with aura and those without.

Table 14

Difference in Response to Treatments A and B Between Subjects with Aura and Those Without.

	Change with T.A.	Change with T.B.
Subjects with Aura n = 29	30.48%	20.37%
Subjects without Aura n = 9	27.78%	27.38%

The advantage of using this structure for the data is that Treatment effects are measured across Treatment groups. For example, some subjects with an aura were in Group 2 and had Treatment A first, some were in Group 3 and had Treatment A second. It has been shown that treatment order has no effect and so it is permissible to ignore grouping by Treatment condition. If Group had to be included in the model at this stage numbers in each cell would be very small. There were, for example, only 3 patients in

Treatment Group 2 who had no aura. When 'No aura' patients from Group 2 are added to the 'No aura' patients from Group 3, there are 9 of them. The disadvantage is that it is not possible to use analysis of variance when the data are in this form because assumptions are violated. This means that the source of any differences cannot be detected statistically. Chi-squared, however, using the method describrd by Meddis (155), is applicable and the source of any significant differences can be identified by a process of elimiation since it is already known that the effectiveness of each Treatment is similar (see Chapter 6). Any differences, therefore, must be attributable to the effect of the variable 'Aura' or to an interaction between 'Aura' and treatment type. The same arguments apply when considering the other two factors of interest, knowledge of'Provocative' factors and 'Independence'.

A chi-squared test was carried out, comparing the cell means with their expected value if Traetment A and Treatment B had exactly the same effect and if presence or absence of an aura was irrelevant. In this hypothetical case the cell means would all have the same value, 26.6%, the overall mean change. The chi-squared value was not significant. It was demonstrated in Chapter 6 that both treatments have the same effect and so if the chi-squared value had been significant it would have been safe to assume that the differences were attributable to the effect of having, or not having, an aura. Within the aura

group, there is a 10% greater change during A than during B. This difference is in the expected direction. The trend supports the hypothesis that experiencing some form of warning before a seizure confers an advantage for Treatment A. It is certainly possible that with a larger sample size it would be possible to demonstrate this statisitically.

b) Auras in Relation to Depression and Seizure Frequency.

The model proposed at the end of the previous section suggests that there could be some unknown factor linking depression to seizure frequency. The next step is to consider whether presence or absence of an aura could be this missing factor. If it is then either its presence or its absence should be associated with high scores on the Zung scale and relatively small change in seizure frequency. It has already been shown that patients who do not experience a warning before a seizure tend to do worse with treatment. Is there any particular reason to hypothesise that they might also be more depressed before treatment? This is a theoretically complex issue in which two possibilities must be considered before forming that hypothesis. It might be expected that patients with frequent seizures which occurred without any warning would be more likely to suffer from "learned helplessness" and as a consequence to have high Zung scores. However the

type of seizure may influence the psychological symptomatology. An aura is a warning of a seizure only from the patient's point of view; in reality it is a part of the seizure itself and the type of aura is determined by the location of the seizure activity. Not infrequently (in this sample approximately 40%) an important component of the aura is a sense of fear or impending disaster. No doubt in some cases this is a psychological response to the imminence of an unpleasant event. In other cases it may be a product of limbic lobe seizure activity. In either case the frequent experience of this unpleasant emotion may elevate the patient's score on the Zung scale. The obvious prediction is that in some cases the absence of an aura would lead to depression while in those cases where the aura itself is emotionally unpleasant there might also be a tendency to depression. Ideally it should be possible to sub-divide the sample into those who experience no aura, those whose aura is mainly affectual in type, and those whose aura consists of some other phenomenon, such as some sensory hallucination. The three groups could then be compared in terms of Zung score. This sub-division is not a practical option because patients find it extremely difficult to describe the beginning of a seizure; by the time all patients who were unable to say with certainty whether or not unpleasant emotion was a significant component of their aura had been excluded, the sample size would be too small for analysis. The sub-division, therefore, remains two-way and the

hypothesis, if it can be called a hypothesis, is simply that either presence or absence of auras may be associated with raised Zung scores.

Table 15 shows the results of a comparison between the two groups, those with an aura and those without, in terms of pre-treatment Zung score.

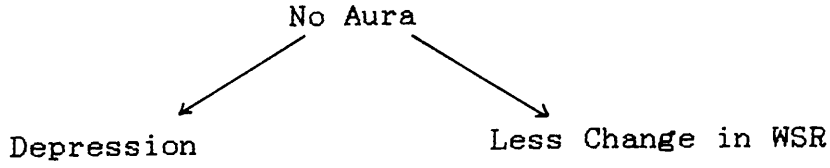
Table 15

Differences in Pre-Treatment Zung score Between Subjects with 'Aura' and those Without.

	ZUNG
With Aura	34.48
Without Aura	49.56

$t = 4.45$ $p < 0.001$

This result suggests that patients who do not have any warning of an impending seizure are on the whole more depressed. They also tend to do less well with treatment overall. It is therefore possible that the following relationship exists:



High Zung score would not, in this case, be a predictor of

poor treatment outcome, and the correlation shown in Table 10 would be spurious. The absence of an aura would be, however, both a predictor of treatment outcome and of Zung score.

2. FACTORS WHICH PROVOKE SEIZURES.

Most patients have theories about conditions, circumstances or events which tend to increase the probabilty of having a seizure. No doubt in some cases the theories are very valid; in other cases they may be self-fulfilling prophecies, and in others simply an effort after meaning without any true relationship to reality. In this sample 35 patients reported that they knew of some factor or factors which tended to increase the probability of having a seizure. The remaining 24 knew of no such factors. The incidence of different factors was similar to that of the preliminary study, with the majority of patients reporting that stress, tension or anxiety 'caused' seizures.

a) Provocative Factors in Relationship to Treatment Response.

These factors may not be of much direct use for seizure interruption techniques since they are generally a much

longer term phenomenon than auras. The stress or tension referred to by patients tends to be a product of some circumstance or set of circumstances. They believe that seizures follow a period of increased stress, or tiredness or hunger or whatever the provocative factor might be. It will be seen that Treatment A deals only with interrupting events, sensations etc. which immediately precede the seizure or which are part of the ictal event itself, not with background provocative factors. If the distinction was absolutely clear then it would be predicted that knowledge of provocative factors would confer no special advantage for Treatment A. If the provocative factors are background psychological problems then they may form a basis for Treatment B to be effective.

There may, however, be some difficulty in determining what is an aura and what is a provocative factor in some cases. Case no. 27 reported that she thought that she was more likely to have a seizure after she had been arguing with her husband. She also reported that she experienced a feeling of unbearable rage and frustration immediately before the onset of a seizure. Cause and effect, and consequently suppositions about the mechanism of treatment, become very mixed in this sort of case. Does quarrelling leading to a particularly intense feeling of rage activate an electrically unstable part of this patient's brain and trigger a seizure? Or do the electrical changes preceding a seizure cause the patient

to become irritable and quarrelsome? If the first is true then a form of Treatment B focusing on improving the management of the relationship to avoid conflicts might be effective. If the second is true then teaching the patient to inhibit or counteract the sensations associated with rage in a form of Treatment A may be effective. In cases such as this where it is not clear whether the so called provocative factor is a 'trigger' or an aura it is not possible to predict whether it will be a predictor of success for Treatment A or for Treatment B.

Table 16 shows the relationship between overall treatment response and provocative factors.

Table 16.

Difference in Treatment Response between Patients who report Provocative Factors and Patients who do not.

Provocative Factors	Mean % change in WSR
N = 35	46.76
No Provocative Factors n = 24	Mean % change in WSR 30.51

t = 1.36 p(1 tail) = 0.09

As in the case when the sample was divided according to presence or absence of an aura, there was no significant difference between the groups in terms of baseline seizure frequency, and the distributions of % change approximated

to normal.

The result shows that there may be a slight tendency for patients who can identify so-called 'provocative' factors to do better, but that the difference is not significant. Given the trend, it is worth sub-dividing response during the two treatments to see whether there is a difference between the groups on one treatment only. Table 17 shows the results of this. It should be noted that the total subject number is smaller than in the above table because only two thirds of the sample have both treatments.

Table 17

Difference in Response to Treatments A and B between Patients who Report Provocative Factors and Patients who do not.

	Change with T.A.	Change with T.B.
Provocative Factors n = 22	19.89%	25.85%
No Provocative Factors n = 16	45.10%	16.76%

$\chi^2 = 27.83 \quad P < 0.001.$

A Chi-squared test was carried out, comparing the cell means with their expected value if Treatment A and Treatment B had exactly the same effect and if presence or absence of provocative factors was irrelevant. In this hypothetical case the cell means would all have the same value, 26.8%, the overall mean change. (Note that this value is 0.2% different than the expected value quoted when discussing the effect of 'aura' on Treatment due to the effect of rounding values off to two decimal places.) The chi-squared value is significant and so it may be concluded that knowledge of provocative factors does influence treatment outcome. It can be assumed that the differences in the cells in the above Table are attributable to an interaction between Provocative factors and Treatment, since it has been shown in Chapter 6 that

both Treatments have an equal effect, and in Table 16 that if patients knowing of provocative factors are simply compared with those who do not, the difference is not significant. It appears, then, that the 'No Provocative Factors' group do better with Treatment A. This finding can probably be explained by the fact that a large proportion of patients feel that stress, anxiety etc. provoke seizures. Treatment B deals specifically with anxiety while Treatment A ignores it. Comparing the STAI scores of the 'Provocative factors' group with the scores of the 'No Provocative factors' group, provides further support for this hypothesis. Data for this comparison are presented in Table 18.

Table 18

STAI Scores for Patients who Report Provocative Factors and Patients who do not.

	STAI (state)	STAI (trait)
Provocative Factors n = 35	46.37	44.63
No Provocative Factors n = 24	61.62	53.98

t(state) = 2.52 $p < 0.01$

t(trait) = 1.72 $p = 0.06$

b) Provocative Factors in Relation to Depression and Seizure Frequency.

Any hypothesis relating knowledge of provocative factors to depression would be rather weak. On the one hand, as in the case of auras, it might be predicted that having no idea of any factor which increased seizure probability, might lead to "learned helplessness". On the other hand knowing of such factors but being unable to avoid them might be more depressing. In any case there is an association between anxiety and depression and anxiety and 'Provocative factors' and so there is a risk that an apparent association between depression and 'Provocative factors' would be spurious. While it might be possible to form a rational hypothesis about any one individual's level of depression if something was known of that individual's circumstances and seizure type, generalisations over the whole sample are unlikely to meaningful. However, a t-test comparing mean Zung score for patients who know of provocative factors with Zung score for those who do not was carried out. The result was not significant. It may be assumed, therefore, that 'Provocative factors do not explain the relationship between depression and seizure frequency.

3. INDEPENDENCE

An 'Independent' patient in this study is one who neither requires nor gets assistance from anyone during his seizures or immediately following them, and keeps he own seizure record. The reasons for including this variable and defining it in this particular way are discussed in Chapter 5. In this sample 27 patients are 'Independent' and 32 are not. Eight patients who were not independent at the beginning of treatment became independent. All of these 8 had more than a 50% reduction in WSR. Since the number who changed their independence is small this variable will be considered as a constant variable.

a) Independence in Relation to Treatment Response.

The 'common sense' hypothesis is that independent patients will be more likely to benefit from self administered treatments. These rely very heavily on self-motivation, and input and supervision by the therapist are minimal. It is unlikely that patients who are unable keep their own seizure frequency records would do as well with this type of treatment as 'independent' patients. This may be because they are less intelligent, have a greater incidence of cerebral impairment, or because they are unused to self-regulation. Table 19 shows mean % changes from baseline to follow-up for independent patients and non-independent patients. As in the case of the other two

factors discussed, there is no significant difference between 'Independent' and 'Non-Independent' patients in terms of baseline seizure frequency.

Table 19

Difference in Treatment Response Between Independent Subjects and Non-Independent Subjects.

Independent (27)	Mean % change in WSR 52.96.
Non-independent (32)	Mean % change in WSR 29.35.

$t = 2.06 \quad p = 0.04$

This difference, although significant and in the predicted direction, is not as large as might be expected when the fact that treatments require a high degree of self-motivaton is considered. Possibly the reason for this is that the influence of a spouse or relative has not been taken into consideration. Non-independent patients, by definition, require support and supervision. It is likely that a spouse or relative will also be active in supporting and encouraging the patient in Treatment A and B. Indeed in both treatments relatives are actually encouraged to participate. Treatment A, however, is the more specific; it does not involve tackling psychological problems which are sometimes long-standing and rather diffuse. Experience in administering the treatments led to the observation that non-independent patients and their

relatives could grasp the principles of Treatment A and co-operate in applying them in much the same way as they co-operate with administring drug-treatments. It was rather more difficult to gain the co-operation of non-independent patients for Treatment B. They perceived this as having nothing to do with their epilepsy and on the whole were more unhappy with the therapist's avoidance of discussing their seizures during Treatment B. It is predicted, therefore, that non-independent patients will have a smaller change in seizure frequency during Treatment B than during Treatment A, and that this will explain a large part of the difference between the Independent and Non-Indepedent groups shown in Table 19.

Table 20

Difference in Response to Treatments A and B Between 'Independent' Subjects and 'Non-Independent' Subjects.

	Change with T.A.	Change with T.B.
Independent Subjects n = 19	27.86%	35.73%
Non-Indpendent Subj. n = 19	31.83%	10.32%

$\chi^2 = 17.14$ $p<0.001$

A chi-squared test, comparing the cell means with their expected value if neither treatment nor independence influenced outcome, that is, the overall mean 26.7%, was significant. As predicted non-independent patient's poor response to Treatment B appears to be responsible for this difference.

b) Independence in Relation to Depression and Seizure Frequency.

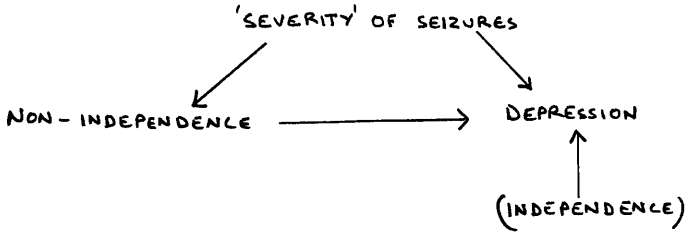
In considering any possible relationship between independence and depression the implications of non-independence must be considered. It is likely that a patient who requires assistance during his seizures has seizures which are in some sense more "severe". In this sample generalised seizures are relatively rare, but a tendency to fall or to wander off during an attack or to carry out some bizarre automatism, is more common. (see

section dealing with type of epilepsy in Chapter 9). In the case of this group of patients any depression would not necessarily be due to lack of independence per se, but to the distressing nature of the attacks. If, however, it were possible to separate patients into two groups by some objective criterion into those who require supervision and those who do not, it would be seen that the correspondence with Independence was inexact. Many patients who get assisstance during a seizure may not require it in terms of the hypothetical objective criterion. Similarly some patients who have a tendency to fall and injure themselves during a seizure declare that they are quite independent. There may, therefore, be a sub-group of patients who are depressed as a direct result of non-independence. A discussion of the theoretical issues linking lack of independence with depression is beyond the scope of this study but since patients have little knowledge of what actually happens during their seizures many find the solicitations of a caring relative uneccesary and frustrating. Others simply become helpless and dependent. Either frustration or dependence could produce depression in the sense in which it is measured on the Zung scale.

There is one other possibility that must be mentioned before forming a definite hypothesis. What of the patients who are Independent because they have no-one to look after them and who feel this as a depressing lack? Among the 40 patients who scored above the criterion on the GHQ and who

were consequently assessed in detail with respect to their psychological background, only 2 appeared to be depressed as a result of unwanted Independence. This possibility can therefore be ignored where the purpose is simply to make a generalisation about a possible link between non-Independence and depression.

The diagram may serve to clarify this relatively complex discussion.



It will be seen that the argument leads to a prediction that non-Independence will be associated with higher scores on the Zung scale than Independence. Table 21 shows the results of a comparison between the two groups, Independent and non-Independent, in terms of pre-treatment Zung score.

Table 21

Differences in Pre-Treatment Zung score Between Independent and Non-Independent Subjects.

	ZUNG
Independent (20)	33.40
Non-Independent (20)	42.35

t = 2.38 p(1 tail) = 0.012

Thus it has been demonstrated that non-Independent patients tend to do less well with Treatment B and that they tend to be more depressed. Non-Independence may, as well as lack of an aura, explain the anomalous results concerning the relationship between depression and treatment outcome. The inter-relation between these variables is becoming complex; discriminate analysis will be used to determine their influence on treatment outcome when they are considered together rather than seperately. Before carrying this out, however, the potential predictive value of the remaining 'demographic' variables must be evaluated.

CHAPTER 9

DEMOGRAPHIC VARIABLES AS PREDICTORS OF TREATMENT REPONSE.

1. AGE

2. SEX

3. MARITAL STATUS

4. TYPE OF EPILEPSY

These variables require only brief consideration because they are of no particular relevance to any treatment mechanism theory. They may, however, have an incidental effect on treatment response, and before selecting the best combination of variables for predicting outcome it is important to exclude the possibility that any one of the variables which might be termed 'demographic' is having a significant effect.

1. AGE

The age range of the treatment sample is 16 to 60 with a

mean of 31.9 years and a standard deviation of 12.2 years. Thus the whole of the adult population is represented with the exclusion of the elderly. Within this range certain changes in responsiveness to treatment might be expected. Older patients might possibly be a little more rigid and less inclined to accept the suggestion that a physiological event, such as a seizure, might come under psychological control. The fact of having a longer history of seizures might disincline them to this point of view. If this were the only age related factor then it would be hypothesised that the patients whose WSR decreased most during treatment were younger. However age is closely related to some of the other variables (independence, for example) which might act in the opposite direction, making this hypothesis rather facile. In fact a groups comparison t-test showed no significant difference in mean age between the patients whose WSR reduced by 59% or more (the "best" third) and those whose WSR reduced by 26% or less (the "worst" third). Neither was there a significant correlation between age and percent improvement in WSR.

2. SEX

In this sample there were 26 males and 35 females evenly distributed amongst the three groups. It might just be possible that sex could have an effect on outcome through an interaction with the sex of the therapist. It is widely

accepted that therapist variables can influence treatment success and that the sex of the therapist is more or less influential depending on the type of therapy. In some cases a male therapist is perceived as being more competent, particularly by male patients, and in other cases a female therapist is perceived by female patients as being easier to talk to. It might therefore be hypothesised that female patients will respond best to treatment, perhaps particularly in Treatment B where discussion of personal matters is necessary. A Chi-squared test shows that there is no difference between the proportion of males in each of the two outcome groups as defined above.

3. MARITAL STATUS

The preliminary study showed an interesting relationship between marital status and GHQ; that is that married patients tended to have higher GHQ scores. The following relationships might be postulated:
Married > GHQ > WSR. However the weakness in these relationships has already been demonstrated and it seems very unlikely that this mechanism exists to any significant degree. Even if it did, the effect on WSR would be constant so that it would not necessarily influence change in WSR in either direction. Before rejecting marital status as irrelevant it is necessary to

consider the usefulness of a spouse as a co-therapist. In treatment A a relative, frequently a spouse was given instructions to help the patient interrupt his seizures and to remind him what he was supposed to do. It might therefore be expected that treatment A would work better if the patient were married. In fact 'Independence' is a more relevant variable in this context since only patients who were not 'independent' would have a relative on hand to give advice during seizures. Many married patients were independent in this respect and many unmarried were not. The hypothesis, then, is that marital status will not affect treatment outcome. Results of data analysis confirm this; there is no difference between mean change in WSR between married patients and unmarried patients. A chi-squared test comparing number of married patients in each of the two categories of improvement also showed no difference.

4. TYPE OF EPILEPSY

It is well known that seizures of a centrencephalic origin can be more readily controlled by pharmacological means than seizures with a focal origin. Secondary generalisation of partial seizures can usually be prevented effectively by drugs. The primary implication of this for the present study is that since the sample by definition is poorly controlled, most patients will have

some form of partial epilepsy. This is indeed the case: reference to Table 5. will show that 26 patients have partial seizures only, 29 have partial seizures with occasional secondary generalisations, and that in 4 cases it was not possible to define the seizure type. No patients had primary generalised epilepsy. Essentially, in terms of the definitions used, 'type of epilepsy' divides patients into only two groups; one with and one without occasional secondary generalised seizures. If these seizures had occurred frequently then it would have been possible to see if psychological treatments were more effective against one type than another in any given patient. Unfortunately from the point of view, of the 29 patients who had generalised seizures the highest frequency was 1 per month and the mean frequency 1 in six months. This is too low to compare teatment effectiveness within subjects. The two groups can be compared in terms of mean % change in WSR, in case there is some inherent difference between them; results showed no significant difference in mean % change in WSR between the groups.

The most important question to be considered is whether psychological treatment is simply eliminating non-epileptic seizures. Possibly, despite the criteria of patient selection, the sample contains two groups, those with epileptic seizures and those with pseudo-epileptic seizures, this division cutting across the division discussed above. If there were two distinct groups with

treatment being effective against non-epileptic seizures only, then one would expect the distribution of the variable % change in WSR to be more binomial than normal. Figure 5 demonstrates that this is not the case.

An alternative possibility is that all patients have epileptic seizures but that a large proportion have pseudo-epileptic seizures as well. Figures as high as 26% have been cited in the literature (94). Treatment could be effective only against these non-epileptic seizures and still result in the same distribution of treatment success. Although some proportion of the seizures eliminated by treatment may be non-epileptic there are a number of reasons why this is not a satisfactory explanation for the whole treatment effect. If the treatments in the study are only effective against pseudo-epileptic seizures then in order to create the size of treatment response - a 50% improvement in 50% of cases - we must assume that most of the sample were having mostly pseudo-epileptic seizures at the start of treatment. It can be imagined that secondary gain may maintain a high seizure frequency in some individuals but it seems unlikely that this could occur in over half of a randomly selected sample given that the highest estimate in the literature is 26%. In any case neither treatment aims to eliminate secondary gain: Treatment B may do so indirectly, but Treatment A not at all. Fenton (90) suggests that the treatment of pseudo-epileptic seizures

is complex, should be carried out in a in-patient setting and requires follow-up over several years. It seems unlikely that the short simple treatments employed in this study could be effective against non-epileptic seizures. Given these arguments it is reasonable to accept that psychological treatments eliminate genuine epileptic seizures. They may eliminate non-epileptic seizures as well, but they are not specifically directed against these any more than are pharmacological treatments.

It may be concluded that neither age, sex, marital status, or type of epilepsy are predictors of treatment reponse and that they may safely be ignored in further data analysis.

CHAPTER 10

COMBINING PREDICTORS.

The previous three chapters in this section have identified some factors which are associated with treatment success or relative lack of success. These are pre-treatment score on the Zung scale, presence or absence of auras, presence or absence of 'provocative' factors and 'independence'. Although these factors show a significant relationship with % change in WSR, individually they are not of much pratical use in predicting treatment outcome; they explain a relatively small proportion of the variance in % change in WSR. As discussed in Chapter 8 the apparent relationship between an initially high Zung score and poor reponse to Treatment B is in any case probably spurious. There is evidence that the apparent advantage of lack of provocative factors is simply a result of the fact that there is a strong association between knowledge of provocative factors and anxiety. However it is worth examining the possibility that some combination of variables is a useful predictor of outcome. This combination should include the three individually significant variables. It might also include 'Provocative factors', which failed to reach significance but which for theoretical reasons could be relevant.

The most sensitive and efficient statistical tool for this type of problem is discriminant analysis. The concept underlying discriminant analysis is fairly simple. Linear combinations of independent variables - that is the possible predictor variables - are formed and serve as the basis for classifying cases into one of two groups, in this case good outcome and poor outcome. For the linear discriminant function to be 'optimal' that is, to provide a classification rule that minimises the probability of misclassification, certain assumptions about the data must be met. Each group must be a sample from a multivariate normal population. SPSSX's "DISCRIMINANT" package carries out Box's M test, which is based on the determinants of the group covariance matrices. The significance probability is based on an F transformation. A small probability would require rejection of the null hypothesis that the covariance matrices are equal. The test is also sensitive to departures from multivariate normality so that it tends to call covariance matrices unequal if the normality assumpton is violated. In each of the discriminant analyses which follow a Box's M test was carried out and in each case the significance level was rather borderline, that is between 0.05 and 0.06. The most likely reason is that some of the independent "predictor variables" are not near enough to normal. A further problem is that some of the variables (Independence, Aura, Provocative factors) are dichotomous. Gilbert (156),

however, concludes that most evidence suggests that linear discriminant function performs quite well with dichotomous variables. Mixtures of dichotomous and continuous variables are less promising. It is apparent that the data are not absolutely ideal for the use of discriminant analysis, but it was decided that since the method has so much to offer it would be used, but that the significance of results would be regarded with some degree of caution.

Discriminant analysis can separate cases into two groups by calculating one discriminant function which maximises the ratio of between- to within- groups sums of squares. If there are more than two groups, one less discriminant function than the number of groups, is calculated. A two group division seems the most appropriate; the results fall more naturally into two groups, poor and good outcome, than three - poor, moderate and good. The division was made along the 50% line so that one group contained 32 subjects who had had less than 50% improvement in WSR and another which contained 27 subjects who had had a 50% or more improvement in WSR.

Discriminant analysis was carried out using eight variables: all four pre-treatment scores on the psychopathology measures, score on the Activities scale, Independence, presence or absence of auras and knowledge of factors increasing seizure probability. A stepwise

variable selection procedure was used, with the criterion for variable selection being to minimise Wilks' lambda. Wilks' lambda is the ratio of within groups sum of squares to total sum of squares. The closer that lambda is to 0 the greater the proportion of total variability attributable to differences between the means of the groups. The variables entered after 4 steps are 'Independence', 'aura' and the pre-treatment Zung and State anxiety scores. The remaining variables did not reach criterion for entry after four steps. Table 21 gives Wilks' lambda values after each of the variables has been entered. The order of the variables is according to the size of their effect, from largest to smallest.

Table 21

Variables used to discriminate between two outcome categories: change in WSR above 50% and below 50%.

VARIABLE	WILKS' LAMBDA	SIGNIFICANCE
1. Independence	0.899	0.014
2. Aura	0.859	0.014
3. Pre- ZUNG	0.829	0.015
4. Pre- STAIS	0.791	0.012

The classification results, using discriminant function scores based on the above variables, show that 68.7% of patients with "good" outcome are classified correctly, and

that 74.1% of "poor" outcome patients are classified correctly.

Returning to the mean score on the four key variables it is seen that being independent and experiencing a warning of a seizure are good prognostic signs and that high state anxiety and a high depression score are bad prognostic signs. The point of discriminant analysis is, of course, that these variables are only of use in predicting outcome when taken together. In fact given the 60 - 70% hit rate it will not be practical to exclude patients from treatment by their score on the discriminant function; there would be too many false classifications. The results do, however, tend to support part of the original hypotheses: 'Independent' patients do indeed do better and so do patients experiencing auras. Highly anxious and depressed patients do not do well; the implication is that they might need more intensive prolonged treatment to bring their symptoms under control.

The definitions of "good" and "poor" so far have been completely arbitrary. It is not usual to define an improvement of less than 50% as a poor outcome. The whole procedure was repeated using subjects towards the ends of the distribution shown in Figure 5. The new groups were "good" with 19 subjects who improved by 59% or more and "Poor" with 18 subjects who improved by 26% or less. It was considered that these were the minimum sized groups

for analysis. Again four variables had a sufficient F-to enter in the stepwise analysis and are displayed in Table 22.

Table 22

Variables used to discriminate between two outcome categories: change in WSR above 56% and change in WSR below 26%

VARIABLE	WILKS' LAMBDA	SIGNIFICANCE
1. Aura	0.823	0.009
2. Pre-Zung	0.715	0.003
3. Pre-STAIS	0.671	0.004
4. Activities	0.636	0.006

It will be seen that 'Independence' is no longer important, but that score on the activities scale is. Using these function scores the classification rate is 83.3% "Good" outcome patients correctly classified and 78.9% "Poor" outcome correctly classified. The result is much better than in the first analysis; the final lambda after four steps is down to 0.631, showing that a relatively larger proportion of the variance is attributable to group differences. In practical terms this means that a patient who does not consider himself to be banned from more than two activities, who experiences some warning of a seizure and who has a State anxiety score of

less than 54 and a Zung depression score of less than 28 is very likely to improve by at least 50% with treatment. It should be noted that a State anxiety score of 54 is almost 2 standard deviations above college student norms and so the treatment can obviously cope with relatively high anxiety levels. The inverse of these factors predicts a poor outcome and so in reality a depressed, restricted patient who never knows from one minute to the next when he might have a seizure is not likely to benefit from treatment. Those falling between these categories may or may not benefit.

These predictor variables are not in any way surprising; they could have been assumed without any complex statistical analysis. Discriminant analysis has not added significantly to the information obtained by examining each variable independently. However the classification rates show that these variables, taken in combination, are reliable indicators of treatment success and failure, albeit only in the top and bottom third of outcome range. Chapters 7, 8 and 9 examined the theoretical aspects of the effects of these variables on outcome. Discriminant analysis has given an indication of their quantitative effect.

CHAPTER 11

LIMITATIONS, CONCLUSIONS AND FINAL EVALUATION.

1. LIMITATIONS

2. CONCLUSIONS

3. FINAL EVALUATION

1. LIMITATIONS.

Inevitably in a clinical study of this kind there are problems in making precise definitions of samples and experimental treatments. Although all subjects in the study had some form of partial seizure, there was a great deal of individual variation in seizure type and in type of psychological difficulty. As a result of this treatments were defined within rather broad limits to cater for the variance in type of problem treated.

Seizure frequency may appear to be a precise, objective outcome measure since it may be thought that either the subject has a seizure or he does not. Error must be

expected, however, in any experiment where the main outcome measure is based on subjects' self-report and not on direct observation. There may be a tendency to under report seizures to please the therapist, and although where possible relatives were involved in seizure reporting, sometimes subjects kept their own records and it must be expected that some seizures would be forgotten. In some cases the relative or patient may not be sure whether a seizure has occurred or not. One of the unmeasured effects of treatment was that patients often reported that seizures had become shorter and less intense. This evidence in itself might lead to less accurate recording, and also throws into question the validity of seizure frequency, rather than duration or severity as an outcome measure. The other outcome measures were standardised questionnaires and so may be assumed to be reliable. The question must be asked, however, to what extent is a score on an anxiety questionnaire a valid measure of the subjects 'real-life' fears and sources of stress, and to what extent does an improvement in score represent an improvement in ability to cope with stress?

Some other limitations have been discussed elsewhere. It has been noted that the exact proportion of pseudo-epileptic seizures in this sample is unknown. Although it is most unlikely that the whole treatment effect is due to the elimination of pseudoseizures, the uncertainty imposes limitations on inferences about

treatment mechanisms. Unless pseudoseizures can be completely eliminated from the equation it is not possible to measure the importance of psychological disturbance in maintaining epileptic seizures.

Another major limitation is that all treatments were carried out by a single therapist. Precautions were taken to ensure that this did not bias the results; none of the outcome measure required the therapist to make any judgement, but a single therapist study does impose limits on treatment evaluation. Certainly the therapist's ability to "sell" the treatment and to engage the subject's co-operation must be an essential ingredient to treatment success. It is at least possible that there would be considerable inter-therapist variability in this and that the same study carried out by a different therapist may have led to more or less successful results. Only in a study using a number of therapists would it be possible to measure this effect.

The failure to control for, or remove these unwanted factors is probably inevitable in this type of clinical experiment. It might have been possible to design a more tightly controlled experiment in a 'laboratory' setting. The present study, however, was designed from a clinical rather than an experimental perspective. It was not intended to provide a definitive answer to the question of how psychological variables affect seizures, but to

provide a definitive answer to the question of whether or not psychological intervention is of any practical use in the management of epilepsy. To be of practical use treatments must be applicable to a clinical population in a clinical setting. Generality is more desirable than precision in makink an initial assessment of the usefulness of treatment. However, within these limitations it has been possible to design and execute a controlled study evaluating two distinct treatments separately and together, and to draw a series of conclusions.

2. CONCLUSIONS.

Conclusions have been drawn throughout the study but have been derived from the discussion immediately preceding them and there has been little attempt to make major generalisations. In this section all previous conclusions are summarised and the arguments which led to them briefly reiterated. (Some compression is unavoidable in summarising complex arguments and where appropriate the reader is referred to the relevant sections may be necessary.)

In the first three chapters of this study a review of the literature showed that pharmocalogical management of epilepsy is not adequate for a significant proportion of patients, either because it fails to control seizures, or

because an exclusively pharmacological approach has no impact on the many psychological and psycho-social problems of epilepsy. A review of studies using non-pharmacological methods of seizure control suggests that some techniques may be effective but that more, and properly controlled, studies with larger numbers of subjects are necessary to evaluate the usefulness of such methods.

In chapter 4 a study of the characteristics of a population of patients with epilepsy attending out-patient Neurology clinics formed the practical and theoretical basis for treatment selection and for the design of the treatment study described in chapter 5.

Chapters 6 - 10 presented the results of the treatment study. There was a significant decrease in seizure frequency during the experiment. This occurred during the treatment phases and not during baseline or follow-up. Seizure frequency did not increase significantly during the six month follow-up period. About 50% of patients had a 50% decrease in seizure frequency.

Group 1, the group with no significant psychopathology, did as well with one treatment as Groups 2 and 3 did with two treatments. Two models are proposed which could explain this finding. One suggests that Treatment A, which teaches interruption strategies, can only be effective

after Treatment B has alleviated psychological disturbance. This model is rejected on the grounds that Group 2, who had Treatment A then B, did not do better than Group 3 who had Treatment B then A. The other model is presented algebraically and suggests that Treatment A brings about a smaller effect in Groups 2 and 3 than in Group 1 because the seizure-precipitating factors against which it is effective, form a smaller proportion of the total number of such factors in Groups 2 and 3 than in Group 1.

Within Groups 2 and 3 both treatments are equally effective and there is no significant order effect. This raises the possibility that in some sense they are the same treatment. It is unlikely that the improvement is simply a placebo effect since it occurs only during active treatment and is maintained during follow-up. It is suggested that their common factor is reduction in passivity and improved sense of self-control.

In addition to the improvement in seizure frequency, Groups 2 and 3 showed highly significant improvements in measures of anxiety and depression and all three groups showed a reduction in the number of work related and social activities they felt barred from as a result of their epilepsy. It is noted, however, that at the end of treatment the overall mean weekly seizure rate is still above 2 and that scores on anxiety and depression scales

remain above 'normal.'

Significant correlations were shown between amount of change in seizure frequency during Treatment B and amount of change in scores on the anxiety and depression scales. An inference is drawn that alleviating psychological distress causes a reduction in seizure frequency.

High pre-treatment scores on the Zung depression scale are associated with less reduction in seizure frequency during Treatment B, even although Zung score falls during treatment. It is suggested that some unknown factor must cause both depression and seizures to be resistant to the effects of psychological treatment. Further evaluation of the data indicates that this factor is likely to be the lack of any warning of an impending seizure, since patients without auras are both more depressed and have a smaller improvement in seizure frequency. Lack of 'independence' is also associated with a poorer outcome and with higher pre-treatment depression scores.

Discriminant analysis showed that the best predictors of a good treatment outcome in terms of fall in seizure frequency, were presence of some form of warning of a seizure, a pre-treatment state anxiety (STAI) score of less than 54, a pre-treatment Zung depression score of less than 28 and not more than 2 activities the patient considers himself barred from. However, discriminant

scores based on these variables correctly classified only 83.3% of patients and should probably not be used to exclude patients from treatment.

3. FINAL EVALUATION.

Putting these various conclusions together it can be seen that both the literature review and the field study show that there is a need for some form of intervention in the management of epilepsy, which improves seizure control in patients refractory to pharmacological treatments, and for some form of intervention which alleviates non-psychotic psychological disturbance. The treatment study shows that intervention with brief, simple psychological treatments can achieve both of these ends. A treatment based on interruption techniques and seizure avoidance brings about a highly significant improvement in seizure control in patients without psychological disturbance and a slightly less significant improvement in patients with psychological disturbance. A treatment aimed specifically at alleviation of psychological disturbance is effective in doing this and in improving seizure control. The results of the study lead to some speculations, and implications for future research, concerning treatment mechanisms.

Treatment A.

The major principle of Treatment A is that subjects are encouraged to believe that they can carry out some activity which can avert seizures. The crucial question is whether they can in fact interrupt seizures or whether the increase in confidence which is a consequence of the treatment is in itself therapeutic.

In some cases, during the course of treatment sessions, it was possible to observe the onset of a seizure, perhaps signalled only by loss of contact with the therapist, followed by the recommended "interruption" strategy, followed by a return to normal responsiveness. Unless the patient is imagining that seizure activity has begun it seems clear that he has really learned to supress it with his physical or cognitive strategy. It might well be possible to confirm this with EEG studies. Ounstead Lee and Hutt (106) reported one case where they were able to alert a child to the fact that his EEG was beginning to show seizure activity. They "punished" this with a noxious stimulus and the child learned to supress the clinical manifestation of the attack. Although the EEG bio-feedback literature is extensive (Chapter 3 section 2), most work is concerned with the effect on overall seizure frequency of learning to increase duation or amplitude of certain cerebral rhythms. To date Efron's 1957 study (130) is the only one showing EEG confirmation of a subject's ability to abort seizures. Efron provides an explanation for the

phenomenon and this is described in Chapter 3. It is also noted that his explanation of a "build up of cortical inhibiton" ahead of the path of the seizure, seems rather simplistic. However without more detailed studies of subjects who are able to abort seizures this explanation is the best available. The mechanism by which an individual can learn voluntary control of autonomic functions such as heart rate is not understood. It is not therefore surprising that the concept of conscious control over neuro-electric activity is still very much in the borderland between science and science fiction. The actual evidence from this study shows only that patients tend to improve if they are encouraged to believe that they can learn self-control over their seizures. The experimenter's observations and Efron's study suggest that in some cases seizure activity is genuinely aborted. This must be shown to be possible using sophisticated recording techniques before satisfactory, testable hypotheses can be produced.

Treatment B.

Psychopathology was measured in terms of standardised anxiety and depression questionnaires. In this sample these appeared to be particularly valid measures since scores were so much higher than normal data (see Chapter 6 Section 4). A major aim of the study was to test the hypothesis that psychological distress can maintain a high

seizure frequency. In the literature review it was reported that such a link has been discussed in a general way (116), but not demonstrated experimentally. It might be theoretically possible, in a laboratory setting, to stress poorly controlled epileptic patients, to record EEG changes, and to see if clinical seizures could be provoked. There would be many methodological, practical and ethical objections to such an experiment on human subjects, but the use of an animal model would overcome these objections. Large numbers of studies investigating the properties of convulsant and anticonvulsant agents in animal models are reported in the literature, but there does not appear to have been any attempt to identify a mechanism by which fear or experimentally produced stress might lower seizure threshold. It has been observed, for example, that cats kindled in the ventral tegmental area show behavioural manifestations of fear (156), but such observations do not support the notion that fear can actually increase seizure probability. As recently as 1986 Delgado-Escueta et al. (157) noted that "We still have no animal model which truly mimics complex partial epilepsies in humans, and the closest experimental version of psychomotor epilepsies in animals is the kindling phenomenon." Perhaps it is this lack which has prevented appropriate investigation of the role of fear, since it is in these forms of the disorder where fear seems the most likely to be a significant factor. The present investigation has been designed to test the negative

corrollary of the hypothesis that fear or anxiety can increase seizure probability; that alleviating symptoms of anxiety, and possibly of depression, brings about a reduction in seizure frequency. This is a most satisfactory option; it can be carried out in a clinical rather than a laboratory setting and so valid clinical generalisations can be made, yet provided the outcome measures are reliable and valid it is a methodologically sound experiment.

Careful analysis of results has shown that although scores on the depression scale fall during treatment, a pre-treatment high score is associated with significantly less improvement in seizure frequency. It was concluded, therefore, that there was unlikely to be a causal relationship between depression and seizure frequency in either direction. (Chapter 7 section 2.)
Symtoms of anxiety and depression tended to occur together and their treatment was not distinct; both were included in the "B" treatment package. This is not an ideal situation for identifying likely treatment mechanisms, but fortunately, due to the elimination of depression as a likely source of poor seizure control it appears that anxiety may be a significant factor. This is a generalisation since there may be patients who have frequent seizures and who suffer from anxiety, yet who do not benefit from anxiety reduction. In this study it was not possible to identify such a sub-group, but its

existence is certainly a theoretical possibility. The STAI and the GHQ show clearly that anxiety falls during treatment, seizure frequency falls during the same treatment, and that there is a correlation between the amounts of change. Since the treatment is designed specifically to alleviate anxiety it may be concluded that doing so directly brings about the improvement in seizure control. Thus there is some support for the hypothesis that anxiety, but probably not depression, can maintain a high seizure frequency.

In the foregoing discussion "anxiety" has been defined entirely in terms of the instruments for measuring it used in this study. The instruments have been selected because they have been shown to be reliable and valid (144), but it is known that subjective anxiety, the physiological changes associated with anxiety and the behavioural accompaniments of anxiety are imperfectly correlated (158). If, as has been suggested, anxiety can in some way cause or maintain seizures, it would be most useful to know which aspect of anxiety is most responsible in order to formulate a hypothesis about how precisely this occurs. There are a number of possible theories. Firstly the link might be explained in purely psychological terms. Suppose, perhaps as a result of leading questions during a clinical interview, perhaps as a result of discussions with other patients, a patient comes to expect to have a seizure if he feels what he recognises as "anxiety". In this case it

might not be the anxiety but the expectation that triggered the attack. If this were the case then we must assume that either a conscious cognition - expectation - can interfere with seizure inhibition, or that patients who believe in the anxiety/seizure link are having a high proportion of pseudo-epileptic seizures. To date there is no experimental evidence that expectation alone can produce genuine epileptic seizures although there is evidence that certain types of cognitive activity can do so (15). The possibilty that the elimination of pseudo-epileptic seizures accounts for the treatment effect in this study has been discussed and it has been pointed out that the magnitude of the effect makes this most unlikely. (Chapter 9).

Secondly the link between anxiety and seizure frequency might be explained in learning theory terms. It might be speculated that there is a form of reflex epilepsy where anxiety, or one of its physiological components, was the "sensory" trigger as in the reading epilepsy or musicogenic epilepsy described by Forster (113, 114). It has been noted (Chapter 3 section 1) that although reflex epilepsies may sometimes respond to desensitisation it is not at all clear whether the stimulus is conditioned or unconditioned. If conditioned then presumably a chance association between the stimulus and a seizure can increase the probability of a seizure occurring at the next presentation of the stimulus. This does not

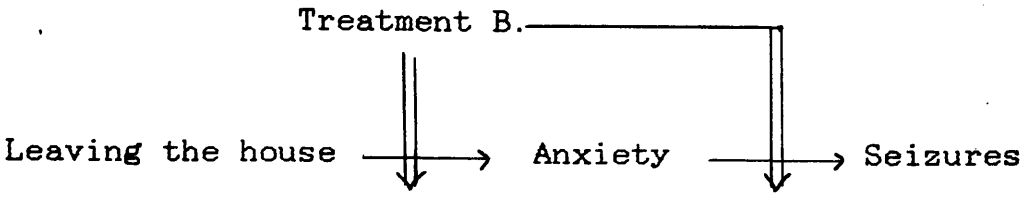
necessarily suggest that there must be some cognitive mediation since it is possible to condition an increase in heart rate to the sound of a bell in utero and to produce many types of behavioural and physological change in response to a conditioned stimulus in relatively primitive animals. Perhaps, then, anxiety is a conditioned stimulus which in individuals with low seizure thresholds might produce seizures as a conditioned "response". If so, the precise neurophysiological mechanism may be similar to that of other learning phenomena. Recent research has shown evidence that the essential conditioned stimulus pathway involves mossy fiber projections and the essential unconditioned stimulus pathway involves climbing fibre projections to the cerebellum. Ablation of these pathways prevents acquisition of certain conditioned resposes (159). At the cellular level it has been shown that learning may be mediated by alterations in membrane permeability (160). Certain predictions about how the CS - CR link between anxiety and seizures would behave should it exist, can be made. It should be possible to extinguish it by desensitisation. Forster (114) has shown that this is possible. In the present study desensitisaton was used not to break the link between anxiety and seizures, but between anxiety and whatever it was causing the anxiety. In most cases the anxiety provoking factor was leaving a safe environment.

As pointed out above, the purpose of this treatment was to

test the hypothesis that reducing anxiety would reduce seizure frequency. It has been shown that it did, but a closer look at the theory that seizures could be a conditioned response to anxiety reveals that this could have happened in two ways.

If the type of desensitisation programme that Forster used (114) was attempted, then the patient would be systematically exposed to levels of anxiety just below the threshold at which seizures were produced, and gradually increasing until the patient was able tolerate levels which previously triggered seizures. This is relatively simple with a sensory stimulus but a little more complicated with such a nebulous set of sensations and cognitions as anxiety. However this may be exactly what is happening during Treatment B. The patient constructs a hierarchy of situations to do with being away from a safe environment and is exposed to them working from the least noxious to the most noxious. This might not only serve to break the link between the anxiety provoking situations and the panicky response, but by repeatedly causing the subject to experience anxiety just below the level necessary to produce a seizure, succeed also in breaking that link. Treatment B, therefore, may produce its effect partly by ensuring that the patient copes more effectively with leaving the house and so is anxious for less of the time, and had less opportunity for having a seizure, but also indirectly by ensuring that higher and higher levels

of anxiety can be tolerated without seizure potentiation.



Thirdly there may be some more direct link between anxiety, or some aspect of it, and seizures. The change in neurological state which occurs when a patient is highly aroused and anxious may interfere with seizure inhibition or may facilitate seizure propogation, or both. The evidence that certain so-called "idling" cerebral rhythms can increase seizure inhibition has been discussed (Chapter 3 section 2). The EEG tends to become more desynchronised during anxiety, with less alpha and more beta rhythm (161), and this may interfere with 'SMR'. Certainly a patient who is trained to produce SMR at will cannot do so at the same time as feeling anxious (117). Anxiety, therefore, may bring about its effect by disrupting inhibitory processes. EEG records only symbolise the underlying neuro-electric processes and so to envisage the direct action of anxiety on seizure inhibition in these crude terms is unsatisfactory. Certain neurochemical studies tend to lead towards the opposite conclusion: that anxiety may actually prevent seizure propagation. Stress raises circulating levels, and brain

levels of adrenaline and noradrenaline, but recent experimental evidences suggest that noradrenaline inhibits seizure activity and may be termed "an endogenous anticonvulsant." (162). There is also evidence from genetic studies of epileptic mice that epileptic strains may be deficient in noradrenaline. The picture is yet further complicated by pharmacological studies showing that although the benzodiazepines most effective in controlling anxiety are rather weak anticonvulsants,(e.g. diazepam), carbamazepine appears to have potential as an antianxiety agent. It has also been shown that there is a long list of convulsant agents which can also produce panic attacks (163). Finally, the fact that some forms of temporal lobe epilepsy and anxiety share a common anatomical substrate in the limbic system is suggestive. It might be speculated that patients with an anxiety disorder could 'kindle' temporal lobe seizures as a result of persistant limbic activity. It will be seen that there is much scope for collaborative work between basic neuroscientists to unravel these various strands of evidence. A direct neurochemical link between seizures and anxiety remains an attractive, but as yet unproven, possibility.

The three theories outlined above which attempt to explain the link between anxiety and seizure frequency are not mutually exclusive. They represent three view-points, one cognitive (expectation), one from the perspective of learning theory, and one from a neurobiological

perspective. This study has provided evidence that a link between anxiety and seizure frequency is likely. Further studies, using more varied anxiety measures such as galvanic skin response and behavioural observations, could pin-point more precisely the sequence of internal and external events which links anxiety and seizures. Telemetric recording of EEG, GSR and heart rate might be invaluable in determining in an individual case whether anxiety was a consequence of seizure onset, part of the seizure itself, or a cause of seizures.

Whether or not these treatments are cost-effective remains a matter of opinion. On the one hand it has been shown that a statistically highly significant effect can be produced with short, simple treatments and maintained for six months. Patients have fewer seizures after treatment than before, they feel less anxious, less depressed and less socially restricted. On the other hand the majority of patients are in no sense 'cured' by the treatment. They remain more psychologically distressed than a normal population and most are still having frequent seizures. Factors predicting treatment success are not sufficiently reliable for use at an individual level. Certainly psychological intervention appears useful in this experiment but it would be unwise to make major claims about it without making two further tests. Firstly, longer

term follow-up should be carried out and if there is a tendency to relapse after six months the effect of occasional 'maintenance' treatment sessions should be evaluated. Secondly, the experiment should be repeated with several different therapists, possibly from a variety of professional backgrounds. If treatment effect can be maintained indefinitely and is generally effective over a wide range of therapists and patient groups, then a good case could be made for including psychological treatments routinely in the out-patient management of epilepsy.

APPENDIX A.

STANDARDISED INTERVIEW SCHEDULE FOR PATIENTS TAKING PART IN PRELIMINARY STUDY

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1. SUBJECT NO: 2. DATE:

3. NAME: 4. ADDRESS:

5. AGE: 6. D.O.B. 7. SEX:

8. MARITAL STATUS:
(Code 1: married/co-habiting Code 2: single Code 3: Other)

9. EMPLOYMENT STATUS:
(Code 1: Employed/student Code 2: Unemployed as a direct result
of epilepsy Code 3: Unemployed for reason other than 2.)

10. MEDICAL HISTORY:
Have you attended any hospital clinics in the past year apart from this one?

11. If so for what reason?

12. Have you ever had any treatment from a psychologist or a psychiatrist?

13. Give reason and approximate dates.

SEIZURE INFORMATION:

14. Type:
(Code 1 = Generalised Seizures, 2 = Partial Seizures, 3 = Mixed 1 and 2
4 = 'Absences' 5 = Unknown.)

15. Frequency per Month: Patient's Record =
Patient's Estimate =
Relative's Estimate =
Case Note Estimate =

16. How old were you when you had your first seizure?

17. How old were you when the diagnosis of epilepsy was made?

Control Rating:

18. Do you feel that the control of your epilepsy on your present treatment is

Good (Code 1)
Moderate (2)
Poor (3)

Patient's rating of control =

If the patient rates control as '3' ask

19. How long since your epilepsy was well controlled ?

20. Neurologist's rating of control =

Record from case records
21. no. of clinic visits in last six months =
22. no. of changes in medication last six months =

23. Can you tell when you are going to have a seizure?

24. How?
(Description of auras, warnings etc.)

25. Do you know of anything which brings on your seizures or anything or circumstance which makes you more likely to have a seizure?
(Description)

26. Do you ever feel that you can put off a seizure or stop one from happening?

27. GHQ 30 score =

28. FSSI score A =
B =
C =
D =
E =

APPENDIX B.

Sample material from 'contract therapy' aspect of Treatment B

A. Patient's list. (In this case 28 year old male.)

Independent: Going to shops
Taking medication
Cooking
Going to pub

Supervision needed : Going to hospital (for out-patient appointments.)

Shouldn't do: Drive
Drink too much

B. Relative's list. (In this case mother)

Independent: Taking dog for walks.
Going to shops for food

Supervision needed: Cooking
Using the lawn mower
Taking medication
Some shopping (i.e.clothes)
Attending for hospital appointments.

Shouldn't do: Drink alcohol
Drive
Use electric hedge trimmer

C) Revised list agreed by both parties.

Independent: Going out for walks
All shopping
Cooking
Going to pub

Supervision needed: Attending for hospital appointments
Taking medication (patient has poor memory)
Using the lawn mower (but mother should watch from the house, not hover anxiously in garden).

Shouldn't do: Use hedge trimmer
Drink more than one pint beer per night.
Drive

APPENDIX C.

1.STANDARDISED INTERVIEW SCHEDULE FOR PATIENTS TAKING PART IN TREATMENT STUDY.

1.SUBJECT NO: 2.DATE:

3.NAME: 4.ADDRESS:

5.AGE: 6. D.O.B. 7. SEX:

8. MARITAL STATUS:
(Code 1: married/co-habiting Code 2: single Code 3: Other)

9. EMPLOYMENT STATUS:
(Code 1: Employed/student Code 2: Unemployed as a direct result of epilepsy Code 3: Unemployed for reason other than 2.)

SEIZURE INFORMATION:

10. Type:
(Code 1 = Generalised Seizures, 2 = Partial Seizures, 3 = Mixed 1 and 2 4 = 'Absences' 5 = Unknown.)

11. Frequency per Week: Patient's Record =
Patient's Estimate =
Relative's Estimate =
Case Note Estimate =

12. How old were you when you had your first seizure?

13. How old were you when the diagnosis of epilepsy was made?

14a. Can you describe one of your usual seizures?
(Patient)
b. How long do they usually last?

15a. Can you describe one of his/her usual seizure?
(Relative)
b. How long do they usually last?

16. Can you tell when you are going to have a seizure?

17. How?
(Description of auras, warnings etc.)

18. Do you know of anything which brings on your seizures or anything or any circumstance which makes you more likely to have a seizure?
(Description)

19. Do you ever feel that you can put off a seizure or stop one from happening?

20a. Do you need any help during or after a seizure?
(Patient)
b. (Relative)

21. Do you always take your medication exactly as prescribed?
Forget occasionally
Forget often
Almost always take less than prescribed

Record from case records
22. no. of clinic visits in last six months =
23. no. of changes in medication last six months =

24. Present medication.

QUESTIONNAIRES:

25. GHQ 30 score =

26. STAI(State) score =

27. STAI(Trait) score =

28. ZUNG score =

29. Activities Check list.

14 to 21 and Questionnaires 25 to 29 were repeated at the end of six months follow up.

APPENDIX C.

2. ACTIVITIES CHECKLIST FOR TREATMENT STUDY PATIENTS.

Tick any of the following activities which you would like to be able to do but cannot do at all, or cannot do as often as you would like, because you have epilepsy.

1. Driving a motor vehicle.

2. Operating machinery and appliances. (machinery at work, or domestic appliances such as motor mowers, electric irons, cookers etc.

3. Drinking alcohol.

4. Making friends/ socialising.

5. Going out alone.

6. Using public transport alone.

7. Going away for a holiday.

8. Career or job which definitely excludes people with epilepsy.

9. Any sport.

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FIGURE 1.

Numbers of subjects in each of 8 Bands
of monthly seizure frequency

N = 151

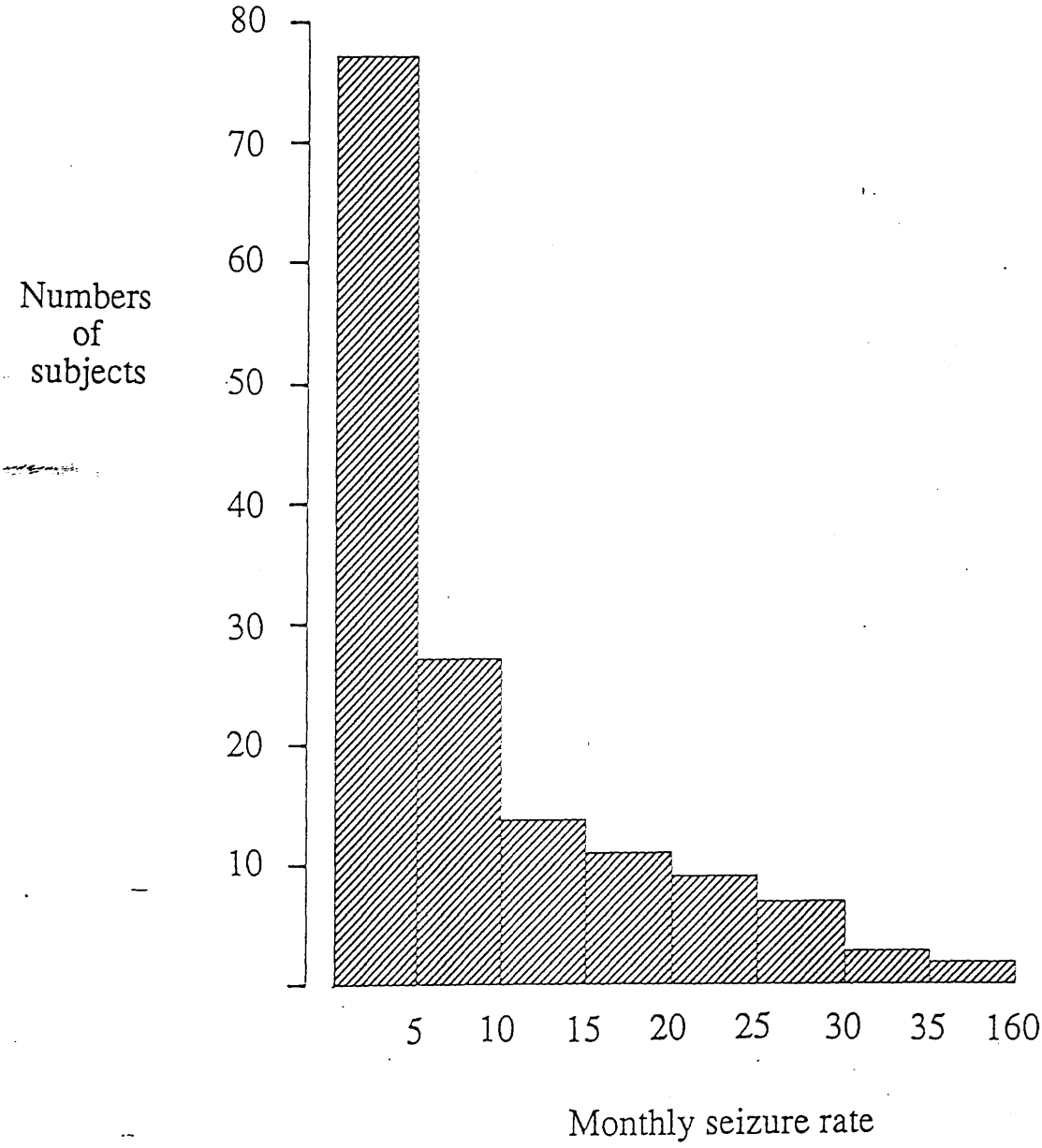
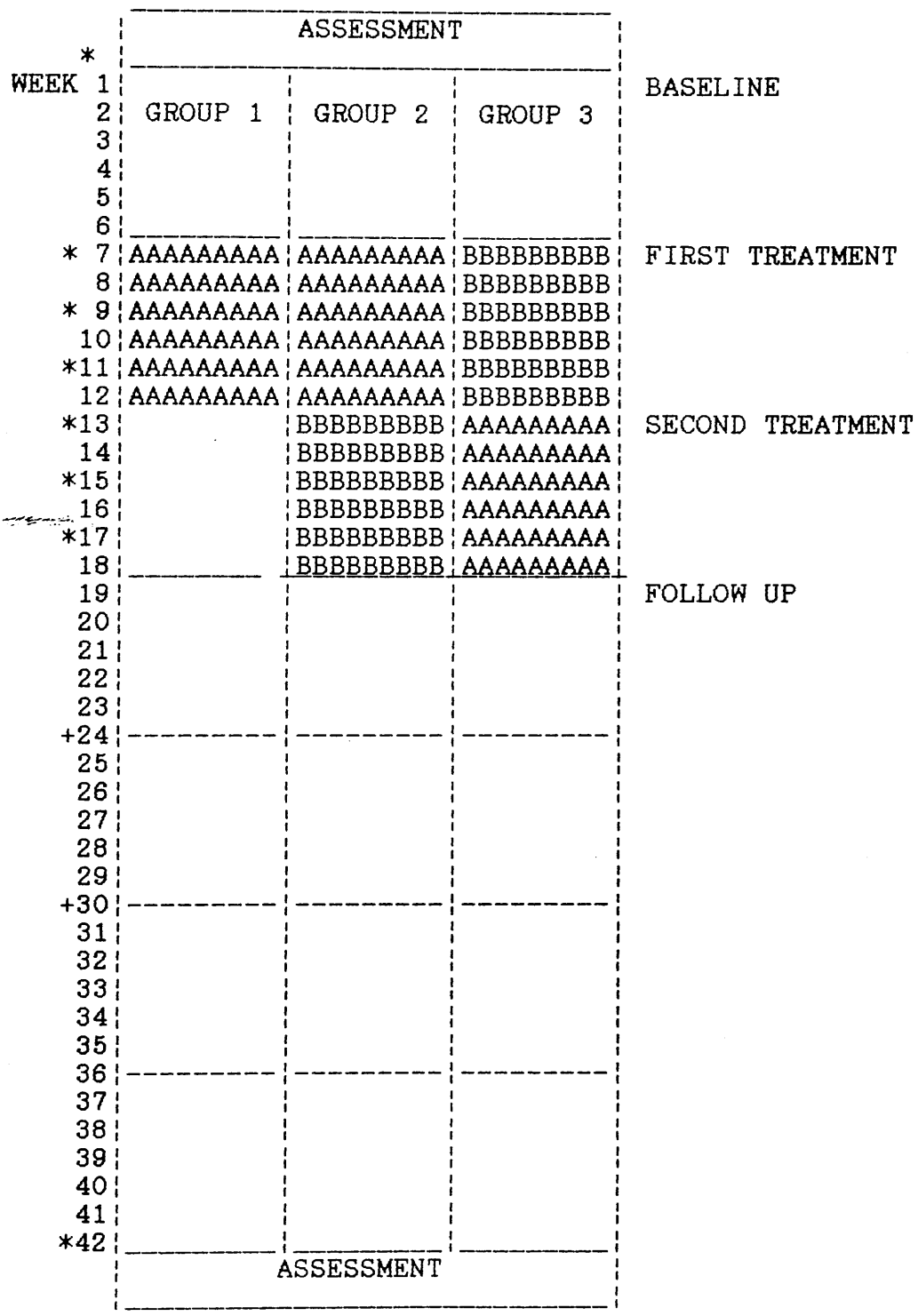


FIGURE 2.

Diagrammatic Representation of the Experimental Design.



* Weeks during which patient was seen by the therapist.
+ During follow up reviews were used simply to collect seizure records.

Mean WSR for each Group in each of the 42 weeks of the study

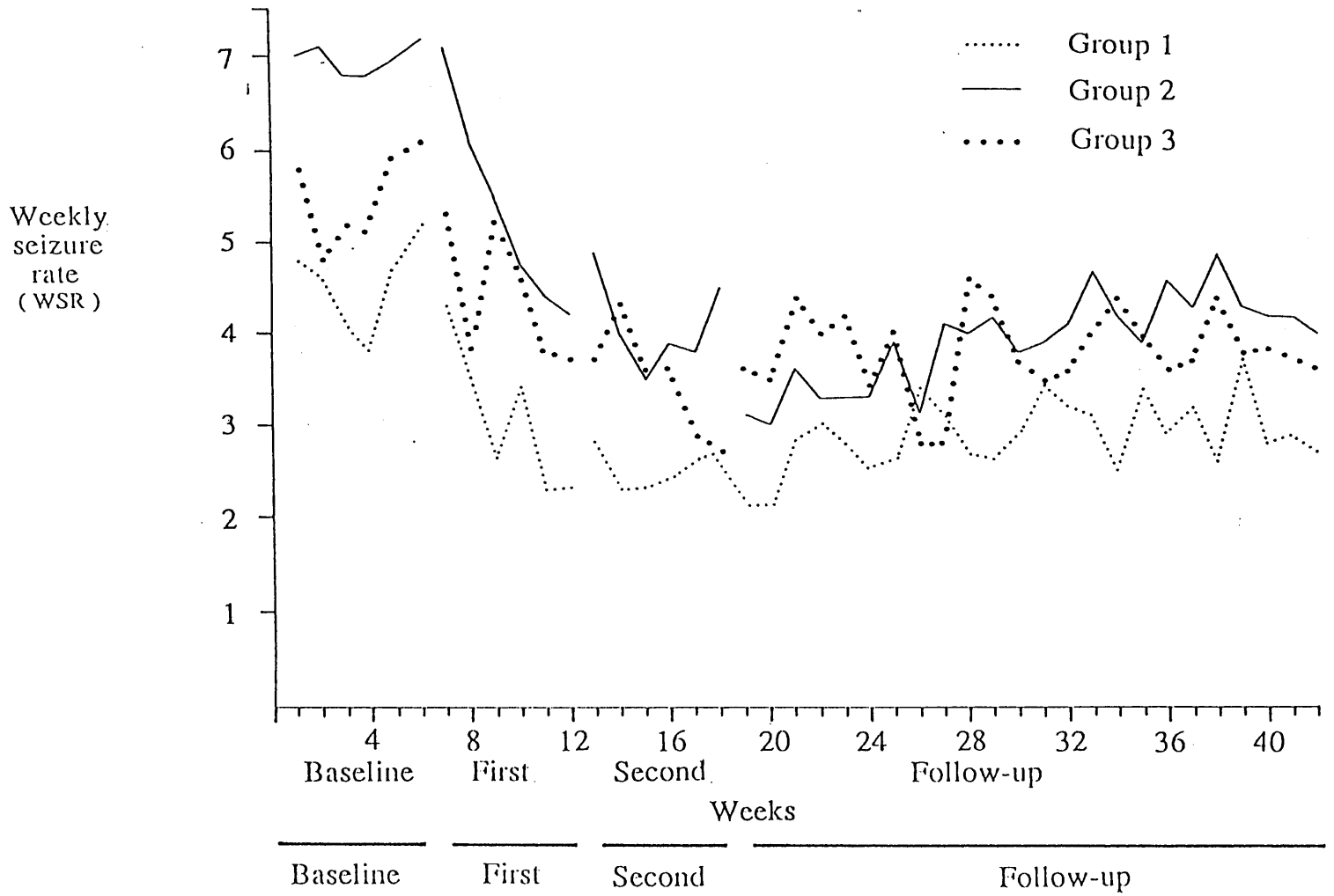


FIGURE 3.

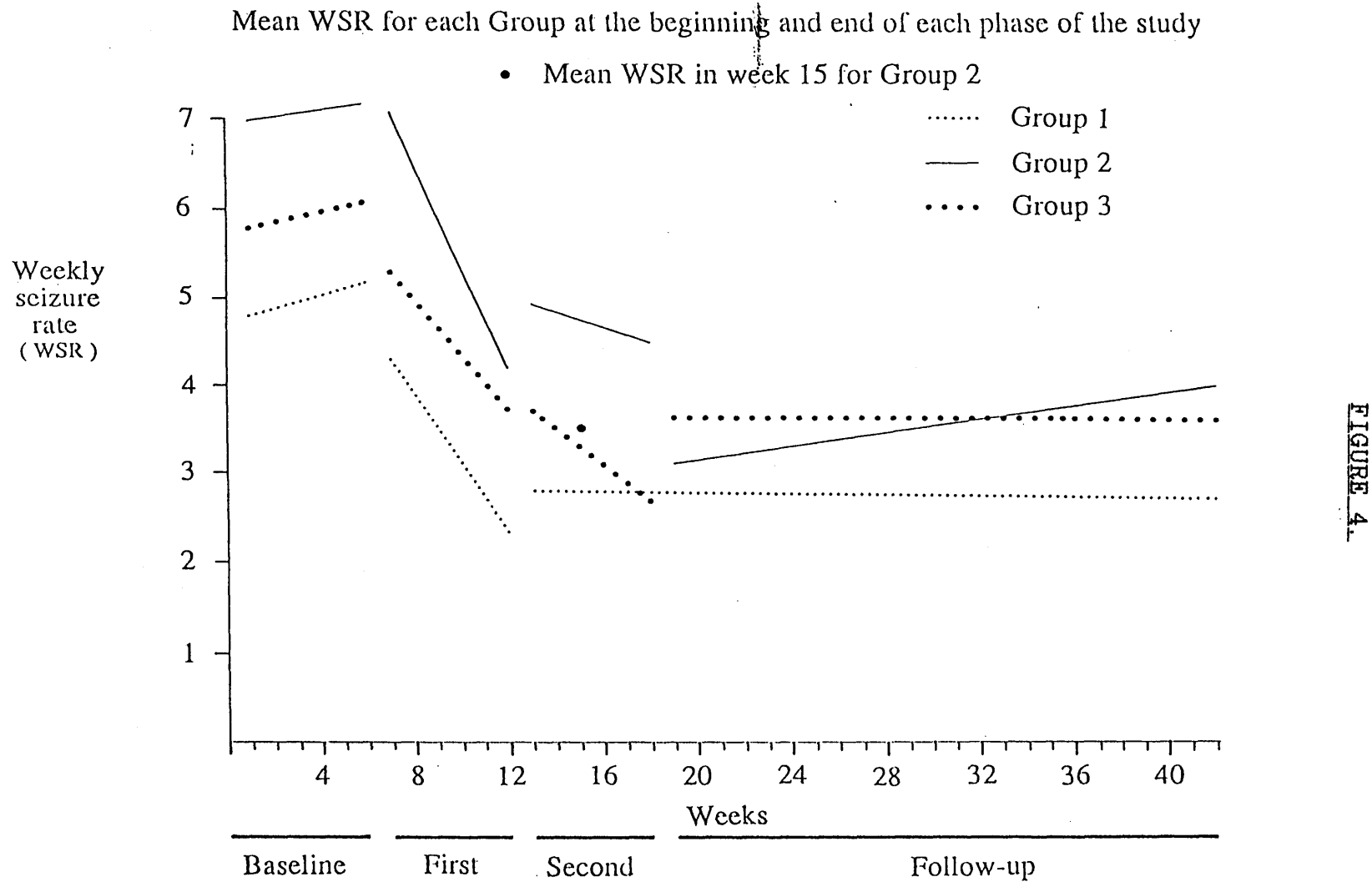

Mean WSR for each Group at the beginning and end of each phase of the study
• Mean WSR in week 15 for Group 2
Group 1
Group 2
Group 3
Weekly seizure rate (WSR)
7
6
5
4
3
2
1
4
8
12
16
20
24
28
32
36
40
Weeks
Baseline
First
Second
Follow-up

FIGURE 4.

Relationships between percentage in improvement in WSR, final follow-up WSR and final control ratings

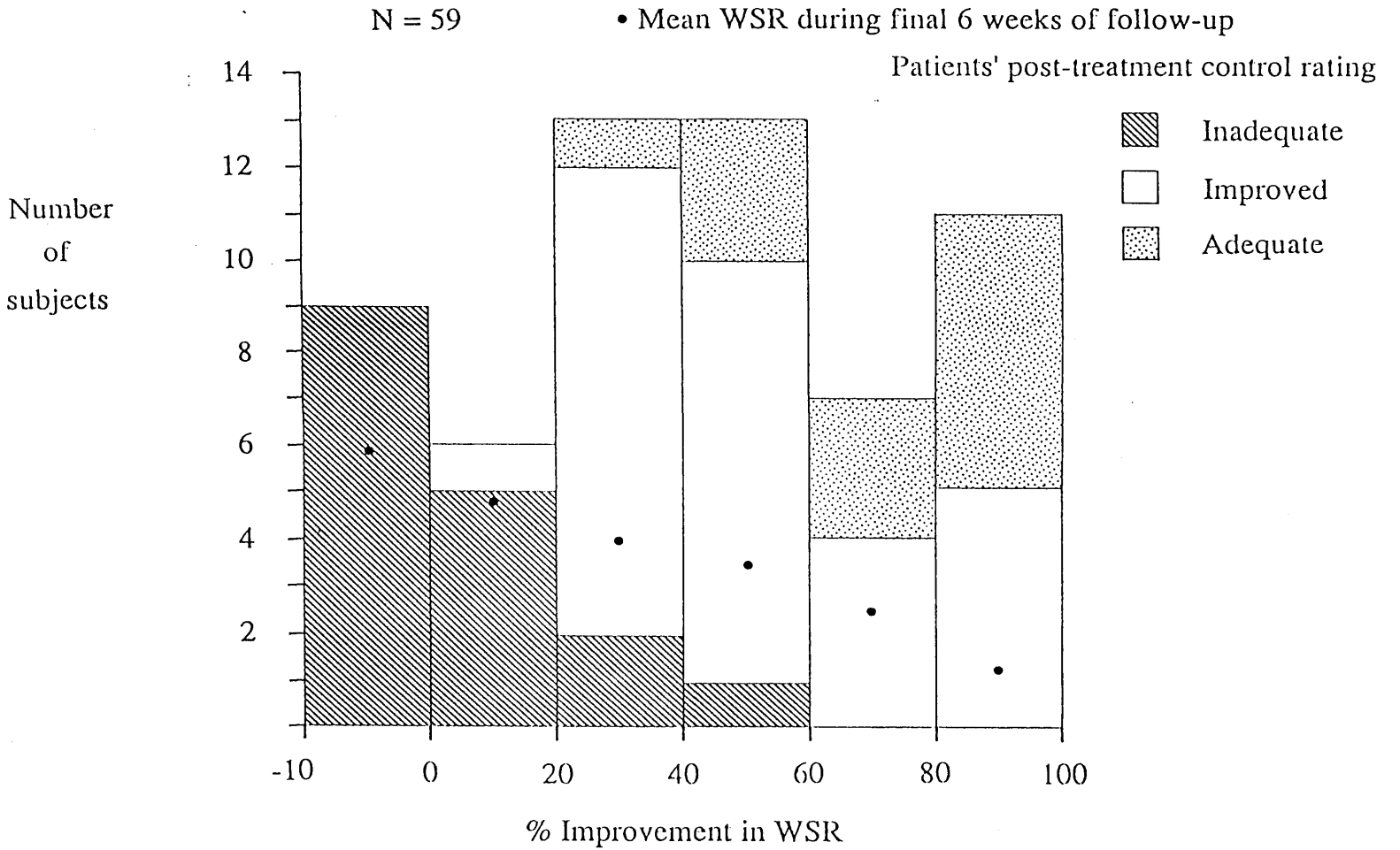


FIGURE 5.