

**SEIZURES DURING VIDEO-GAME PLAY AND OTHER COMMON  
LEISURE PURSUITS IN KNOWN EPILEPSY PATIENTS WITHOUT  
VISUAL SENSITIVITY**

by

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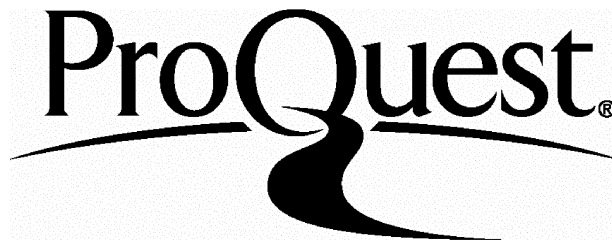
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## **ABSTRACT**

**Purpose:** Some individuals who are negative to flash / pattern sensitivity have been reported to experience seizures whilst exposed to video games. This study sought to systematically examine whether playing video-games is a risk factor for seizures in patients with chronic epilepsy without visual sensitivity.

**Methods:** Two hundred and twelve chronic epilepsy sufferers participated in the study. All were negative to rigorous flash and pattern sensitivity testing. They were randomly allocated to a video game playing session or to a period of leisure (involving reading, physical exercise, puzzles etc) and then alternated between these activities for a fixed total of eight forty-five minute periods whilst undergoing video EEG monitoring. The study ceased if the participant experienced a clinical seizure.

**Results:** 25/212 subject experienced a seizure whilst participating in the study. Thirteen seizures occurred during periods of video game play and twelve during alternative leisure.

**Conclusions:** The present study did not identify a greater risk of seizures in patients with non visually-sensitive epilepsy during video-game play compared with other common leisure pursuits. Furthermore, this investigation exposed a large population (212 patients) mostly with severe epilepsy, mainly drug-reduced and some sleep deprived, to prolonged video-game playing without observing a significant excess in the number of seizures. This finding provides strong support for the hypothesis that seizures during video-game play in the > 95% of the epilepsy population without visual sensitivity are most likely to represent a chance occurrence, although, as always, each individual should be carefully assessed.

### **Statement of Originality**

I was personally responsible for all aspects of this project; including study design, determining which equipment to use, obtaining consent from patients, piloting work, supervision of all (247) study participants, analysis and writing up.

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## 1 History of Reflex Epilepsy

### 1.1 Early accounts of 'evoked' seizures

Consistently accompanying early accounts of convulsions in the ancient texts was speculation regarding their precipitants. Plutarch related that the Spartan women, in order to find out whether an infant was worth weaning, washed it all over with undiluted wine, which would make epileptic and sickly ones fall into convulsions but strengthen healthy ones (Temkin 1971).

One of the three types of epilepsy defined by Galen was that 'due to a sympathetic involvement of the brain originating from any other part of the body'. Evidence for this was thought to be provided by patients who felt a flow of the humors toward the brain (Brock 1929).

Although the general acceptance of a reflex action in epilepsy came fairly recently in the early to mid 19th century, the initial theoretical underpinnings to a general reflex theory are attributed to as far back as the early to middle 17th century.

### 1.2 Reflex Theory

Rene Descartes (1596-1650) explained sensory action by the movement of 'delicate threads' that run from the sense organs to the 'orifices of certain pores which exist on the internal surface of the brain' (Fearing 1930). When external stimuli excite the sense organs they cause a slight pull on these threads which opens the orifices in the brain and thus facilitates the flow of animal spirits to flow toward the muscles.

Figure 1 Descartes' explanation of the mechanism underlying reflex movement



Descartes explains his now famous illustration (see Figure 1) from *De Homine* with:-

*When this pore is opened the animal spirits of the cavity enter into the tube and are carried by it partly to the muscles that pull it back from the fire, partly to those which turn the eyes and the head in order to*

*regard it, and partly to those which serve to advance the hands and to bend the whole body in order to shield itself* (Descartes)

Willis (1621-75) expanded on Descartes idea by explaining the concept of a reflexion in terms of a complete arc from sense organ to brain and back again to sense organ (Kruta 1963). He made a distinction between lower (brain) and higher (cerebrum) nervous centres and believed that the former were responsible for involuntary actions, although reflex action could occur in either of these structures (Fearing 1930).

Robert Whytt's (1714-1766) significant contribution to the area was to demonstrate that the spinal cord was essential for reflex action. He conducted experiments on animals that showed that reflex functions ceased when the spinal cord was severed.

George Prochaska (1749-1820) is credited with combining both existing and his own ideas into a general theory of activity for the nervous system. *Vis nervosa* is the term he used to describe the capacity of the nerves to receive external stimuli and transfer impressions produced by them in either direction at great speed (Kruta 1963). Prochaska postulated the existence of two types of nerves; centripetal and centrifugal. The centripetal nerves were deemed responsible for perception and sensation and were attached to the brain and the centrifugal were responsible for muscle activity and were located both in and outside the brain.

### 1.3 The application of Reflex Theory to epilepsy

The person most commonly credited with introducing 'reflex theory' to epilepsy is Marshall Hall (1790-1857). Tempkin (1971) argues that 'it is certain that only after Hall's communication did reflex action become a widely accepted hypothesis for the explanation of epilepsy'. In 1833, Hall wrote:- 'Epilepsy is plainly of two kinds: the first has a centric origin in the medulla itself, the second is an affection of the reflex function, the exciting causes being eccentric, and acting chiefly upon the nerves of the stomach or intestines, which consequently form the first part of the reflex arc'.

### 1.4 The late 19th century and a reduced status for reflex mechanisms within epileptology

In the late 19th century the concept of 'reflex epilepsy' clearly lost favour as neurologists better understood that seizure activity was localised in the brain. Gowers (1881) states that 'all the phenomenon of the fits of idiopathic epilepsy may be explained by the discharge of grey matter'. 'That there are no facts to warrant us seeking the seat of the disease elsewhere than the grey matter in which the discharge commences, that is in most cases within the cerebral hemispheres, probably often in the cerebral cortex'.

In one of the earliest indications of the prevalence of RE, Muskings (1926) found only one single case out of some 2000 patients treated by him. He argued that RE was therefore a negligible entity and suggested

that the very large number of cases reported in the second half of the 19th century should be put down to a profound lack of criticism (Vizioli 1963).



## 2 Epidemiology of Reflex Epilepsy

### 2.1 Incidence and prevalence studies of Reflex Epilepsy

The proportion of epilepsy sufferers that have their seizures precipitated by a well-defined stimulus or situation still remains somewhat of an uncertainty today. Gastaut and Tassinari (1966) stated that 'induced epileptic seizures' are extremely rare, representing less than 1% of all epileptic seizures. They divided these into four groups:- (i) Seizures provoked by non-sensory triggering factors eg hyperthermia and by excessive alcohol consumption (ii) Seizures provoked by sensory triggering factors eg visual stimuli and startle (iii) Seizures voluntarily induced by the subject itself and (iv) Seizures induced by conditioning stimuli.

Servit et al (1962) asked medical staff from two centres for the treatment of paroxysmal diseases in Czechoslovakia to fill in questionnaires on reflex mechanisms on 895 attending patients based on their past detailed history. Two groups of patients were identified:- (i) in some 40% of patients it was possible to ascertain the influence of stimuli or stimulating situations on the frequency of seizures (either inhibitory or excitatory factors), and (ii) in 5% of the sample one or more certain stimuli could be defined which would regularly or very often initiate a seizure (one third of which was an optical stimulus).

Roger et al (1989) consulted a log-book used to record special syndromes in patients, notably those who were studied polygraphically, at the Centre Saint-Paul between 1960 and 1988. They identified 101

individuals <sup>whose</sup> ~~who~~ seizures were precipitated by a stimulus out of a population of approximately 10,000 (1%). 31 subjects only experienced stimulus-triggered seizures and thus were considered to have reflex epilepsy, the remaining 70 were defined to have epilepsy with reflex seizures as they experienced spontaneous seizures as well. 60/101 subjects had their seizures precipitated by a visual source. The author conceded that this figure was likely to represent a minimum as 'reflex triggering of seizures had not been a criterion for filling in of medical charts over this period'.

Beaumanoir et al (1989) found that a much higher proportion (7.1%) of their study population of 549 epilepsy sufferers experienced their seizures in response to exposure to an external stimuli:- (i) 2.5% were described as having reflex epilepsies stricto sensu - with rare spontaneous seizures and (ii) 4.5% were described as having epilepsy with reflex seizures - with a number of spontaneous seizures. The following strict selection criterion was employed:- (a) appearance of the first seizure before age 11 (b) five years evolution at least until the age of 15 (c) minimum 15 seizures enough detailed itemised in the medical dossier, until the age of 15 (d) several EEG's recorded during the evolution until age 15, with systematic use of homogeneous intermittent light stimulation (HILS) and unexpected sound stimuli (USS), and in some cases pattern visual stimulation. Two thirds of the sample had their seizures precipitated by light.

Oller-Daurella et al (1989) reported 198 patients with 'reflex seizures' in a database covering 5000 individuals with epilepsy, giving a prevalence of ~ 4%.

## 2.2 Problems with epidemiological studies of Reflex Epilepsy (RE)

Epidemiological studies of RE have to overcome several potential difficulties. These may include:-

- (i) problems created by the absence of a universal definition of the condition
- (ii) problems with epidemiological studies in epilepsy generally
- (iii) problems obtaining sufficient proof of a causal link between stimulus / situation and seizure / epileptiform activity

### 2.2.1 Definitions of reflex epilepsy (RE)

There has been a considerable and ongoing debate regarding how RE should be defined. One of the main problems is how to deal with spontaneous seizures. The classic definition, echoed by Henner in 1963, states that 'the term "reflex epilepsy" should be reserved for the rare cases where the epileptic seizures are always provoked by one stimulus and never occur without this stimulus'. However, this definition is seldom adhered to, due possibly to the rarity of such cases. Some investigators have subsequently relaxed their definition of 'reflex epilepsy' to allow a small number or minority of spontaneous seizures (Gastaut 1989). The term 'reflex seizures' has been used to describe

cases where a greater proportion of seizures are spontaneous, with a smaller but definite number involving 'reflex mechanisms'.

A further problem is what types of precipitants to include. The majority of previous studies have tended to include only external modes of precipitation (Penfield and Erickson 1941) which ignore the role of the internal milieu in the generation of seizures (Duncan et al 1995). Antebi and Bird (1992) argue that the term 'reflex epilepsy' should be abandoned or at least have its definition relaxed to incorporate emotional stressors such as anxiety and physiological stressors such as sleep deprivation. They propose the term 'seizure facilitator', which is defined as various psychological states or stimuli which are perceived by patients to have regular association with seizure frequency. However, adherence to such a definition may introduce more problems than it solves. Firstly, the states / stimuli involved are often not well defined, ie there are difficulties in forming general definitions for such states as anxiety and stress (Lai and Trimble 1997). Secondly, the emphasis is on the patient's perception of the 'regularity' of the association between stimulus and seizure. It is possible that some patients may overemphasise what is only an infrequent association between say mood and seizure occurrence.

### 2.2.2 Methodological issues in the study of reflex epilepsy / seizures

Given the rarity of reflex epilepsy, identification of cases from the general population would involve studying large populations, entailing great expense and time. Consequently, virtually all of the few

epidemiological studies of RE have studied a population with known or newly-diagnosed epilepsy.

Epidemiological studies in epilepsy have a number of specific problems (for a comprehensive review see Sander and Shorvon 1987), which will be inherited by any secondary analysis of this population.

### 2.2.3 Establishing Causality in Reflex Epilepsy

A causal association may be broadly defined 'as an association between categories of events or characteristics in which the alteration in the frequency or quality of one category is followed by a change in the other category' (MacMahon and Trichopoulos 1996). The definition of causality has remained a continued source of debate within the philosophy of science since Hume's 'Treatise on Human Nature' was published in 1739. Unsurprisingly, different sciences have different interpretations of how causality should be established (Beagenhole et al 1993). For reflex epilepsy, there needs to be evidence of a reliable relationship in which the presentation of a well-defined stimulus / situation precedes the onset of the epileptic seizure (Commission on Classification and Terminology of the International League Against Epilepsy 1989).

#### 2.2.3.1 Using a patient's clinical history

Most studies have tended to rely solely on the patient's clinical history as it represents the most practical method of obtaining evidence for a

link between stimulus / situation and seizure. However, several issues may present problems.

Firstly, the diagnosis of epilepsy is not as straightforward as other chronic conditions, due mainly to the intermittent presence of its symptomatology. It is likely that in clinical practice both false positive and false negative diagnosis are common (Sander and Shorvon 1987). For example, Lesser (1985) found that approximately 20% of patients referred to specialist epilepsy clinics actually experience non-epileptic attacks. Non-epileptic attacks, which were formerly known as pseudoseizures, are thought to be psychological in origin and are recognised to be more commonly precipitated by external stimuli / emotional states than are epileptic seizures (Trimble 1995). Studies which include or are likely to include subjects that experience such events, ie those heavily drawn from neuropsychiatry clinics, may inflate the proportion of subjects reporting seizure precipitation. Secondly, methods of case ascertainment may promote inaccuracies in the positive identification of epilepsy. The most common method used in published epidemiological studies of epilepsy (Hauser and Kurland 1975) and reflex epilepsy (Roger et al 1989, Oller-Daurella 1989) is that of a retrospective review of medical records. There is likely to be considerable variation both in the way different physicians interpret symptoms and the detail they subsequently record (Sander and Shorvon 1987). This is particularly pertinent in the identification of reflex epilepsy, where physicians may ignore or overstate the importance of seizure precipitants.

Thirdly, the majority of studies of reflex epilepsy rely on self-report from patients. How patients view their illness may affect the likelihood of them reporting precipitants. Illness cognitions have been defined as a 'patient's own implicit common sense beliefs about their illness' (Leventhal 1980, Leventhal and Nerenz 1985). One of the most frequent groups of illness cognitions held by patients concerns the cause of their disease (Lau 1989). Persons with epilepsy often seek an explanation for the occurrence of a seizure or their seizures. Antebi and Bird (1992) state that illness rationalisation ('there must be a reason why I have an attack') may lead to false associations between a seizure and the circumstances preceding it. Epilepsy sufferers may be prone to cognitive distortions such as 'I am unhappy today and have had an attack, therefore any time I have an attack it must be because I am unhappy' (Antebi and Bird 1992). Such a distortion may be widespread. In order to obtain an accurate account of seizure precipitants it appears necessary in most cases to seek confirmation from a reliable witness, although someone closely involved with the patient eg family or carer may share these perceptions (Antebi and Bird 1992).

Fourthly, it is important to determine the frequency of the association between stimulus and seizure. David Hume (1739) wrote:- 'We are never able, in a single instance, to discover any power or necessary connection, any quality which binds the effect to the cause, and renders the one an infallible consequence of the other. We only find that one does actually, in fact, follow the other'. When a greater number of seizures are associated with a particular stimulus the patient's exposure

time to that stimulus needs to be taken into consideration. Gastaut (1962) recognised that a proportion of the 35 cases of 'television seizures' he documented may have been fortuitous, given the prolonged viewing times of some patients. Taking television as an example, a patient with an average seizure frequency of two a week (without diurnal variation) who watches television for only three hours a day can reasonably expect to suffer 13 fortuitous seizures during television exposure annually. Other reports have documented cases where the stimulus in question is frequently encountered during vocational / educational commitments (Mutani et al 1980, Saenz-Lope et al 1985) or leisure pursuits (Herskowitz et al 1984, Brenner and Seelinger 1979). In such cases a more careful analysis of the association may be required. Zifkin (1989) has argued for a greater use of detailed statistical analysis to determine the extent of the relationship between the 'putative epileptogenic stimulus and the occurrence either of clinical seizures or of interictal epileptiform activity'.

Fifthly, for some patients the start of the seizure will be preceded by a warning or aura. This can take such contrasting forms as fear, irritability and pleasure. Patients that do not recognise such sensations as integral to the seizure process may mistake them as precipitating factors.



### 2.2.3.2 The utility of the electroencephalogram (EEG) in the investigation of reflex epilepsy / seizures

The visual reflex epilepsies (eg flash and pattern sensitivity) can in most patients be readily demonstrated during EEG studies provided adequate equipment and methodologies are employed (see false negatives later).

Roger et al (1989) demonstrated visual sensitivity in the laboratory in 54/60 (90%) of patients with a history of environmental visual seizures.

Startle epilepsy, the second commonest form of RE, is less often demonstrated under laboratory conditions. 10/16 (63%) of cases reported by Aguglia et al (1984) and 24/60 (40%) of cases documented by Roger et al (1989) demonstrated evidence of RE during EEG recordings.

Other investigators have achieved far less success confirming a clinical history of RE in the laboratory. Beaumanoir et al (1989) found that only 5/39 individuals with a clinical history of varied types of RE experienced reflex seizures during prolonged EEG investigations. RE's which involve elaborate stimuli, sometimes described as the complex reflex epilepsies (Zifkin and Andermann 1998), can present special difficulties for systematic investigation as the material in question may be multifaceted eg game-playing epilepsy. A further problem for investigators of RE is the inescapable ethical dilemma of deliberately precipitating seizures.

### 3 Seizures during exposure to video game material

#### 3.1 A definition of video game material

The term 'video game' is used by the general public, the media and in the medical literature to describe all types of interactive visual games. These include personal computer and television console games as well as arcade and hand-held varieties. Video game play represents an increasingly common pastime as a leisure pursuit for many individuals, particularly children and adolescents, and it has more recently been utilised in educational and employment settings.

Two years before the first documented case of an epileptic seizure associated with video-game play one group of investigators warned that this material could trigger epileptic seizures<sup>m</sup> certain patient groups. Wilkins et al (1979) stated that 'with the greater use of a television monitor as a medium for interactive visual display terminal', requiring the operator to sit closer than they otherwise would to the display, 'it seems inevitable that the incidence of television epilepsy will increase'.

The first report of a video-game seizure (VGS) was made by Rushton in 1981 after a 17 year old youth experienced a 'grand mal' seizure during exposure to the arcade game 'Astro Fighter'. The attack was reported to have occurred after the subject had been playing the game for some 20-30 minutes. The investigator found that at the conclusion of the game, the screen was filled with a multicoloured stroboscopic effect, flashing

at approximately 15 Hz for two seconds. This scene was subsequently confirmed by the patient as the stage in the game that the seizure took place. It was suggested that flickering light may have been implicated as a possible precipitant of this seizure although photosensitivity was not demonstrated in subsequent EEG studies.

Up until October 1998, there were a total of twenty four studies detailing 213 cases where a seizure has apparently been precipitated by exposure to video game material (Jeavons et al 1981, Daneshmend and Campbell 1982, Dalquist et al 1983, Helfgott and Meister 1983, Glista et al 1983, Wong et al 1983, DeMarco and Ghersini 1985, Ferry et al 1986, Vespignani et al 1986, Ambrosetto and Tassinari 1987, Giroud et al 1987, Hart 1990, Maeda et al 1990, Cook and Hoskins 1992, Henchey and Gilmore 1993, Thompson 1993, Graf et al 1994, Harding et al 1994, Ferrie et al 1994, Allen et al 1994, Kato et al 1994, Takahashi et al 1995, Quirk et al 1995) [see Appendix One].

### 3.2 A known cause of video-game seizures - visual sensitivity

(i) In 55% of documented cases there is evidence to suggest that the **visual content** of the game was the likely precipitant of the seizure. This group of patients responded positively to visual sensitivity testing. The two main types of visual sensitivity are photosensitivity (usually associated with flashing light material) and pattern sensitivity.

### 3.2.1 Photosensitivity - description and epidemiology

Photosensitivity can be an asymptomatic trait or manifest as 'light-induced' seizures if combined with epilepsy. The most common trigger of photosensitive seizures is the television set, although sunlight, disco lights and computer screens have also been implicated (Harding and Jeavons 1994). Intermittent photic stimulation (IPS) during an electroencephalogram (EEG) recording is the established 'gold standard' test for photosensitivity. A photoparoxysmal response (PPR), which is defined as an abnormal response to visual stimulation, is considered evidence for the presence of photosensitivity. A Type 4 photosensitive response has the greatest association with a clinical expression of PSE (Newmark and Penry 1979). The prevalence of photosensitivity has been studied in patients:- (i) attending a routine EEG, and (ii) with known or suspected epilepsy.

Jeavons (1966) reported that 2% of 14,000 consecutive, unselected patients with neurological and / or psychiatric conditions attending an EEG demonstrated 3 Hz spike and wave during IPS. This rate accords with other similar studies (Gastaut 1958, Graf 1980).

Kasteleijn-Nolst Trenite (1989) reported 'generalised spike/polyspike wave discharges' that outlast the IPS in 4.3% of 2342 cases at a centre dedicated mainly (98% of patients) to the treatment of epilepsy. Some reports have found much higher prevalence figures, with up to 17% of

the referred population demonstrating photosensitivity (Covanis et al 1982). However, the referral of patients to a single treatment centre with a known specialist interest in photosensitivity is likely to be biased toward photosensitive cases.

In one of the few studies investigating incidence, Quirk et al (1995) monitored 90% of all EEG's performed on people with newly diagnosed seizures throughout Great Britain over two three month periods. They found that the incidence of PSE was equivalent to 1.5/100,000 of the population, although this rose to 7/100,000 when the age range is restricted from seven to nineteen years. These figures represent approximately two and ten percent of all new cases of epilepsy respectively.

PSE presents most commonly in late childhood and adolescents and affects more females than males (Quirk et al 1995). Sufferers of idiopathic generalised epilepsy are more likely to harbour photosensitivity than those patients with partial epilepsy. Clinically, seizures are most frequently absences and generalised tonic-clonic convulsions. Myoclonic jerks are also found in some individuals but partial seizures are rare (Harding and Jeavons 1994).

### 3.2.2 Video-games and photosensitivity

Video game play can involve exposure to both the inherent flicker of the broadcast medium as well as to any flashing sequences that may be

introduced by software. The television set, which flickers 50 Hertz (refresh rate of 25 Hz) in Europe and at 60 Hertz (refresh rate of 30 Hz) in the United States, is by far the most epileptogenic medium of transmission as it's level of flash frequency, particularly the refresh rate, is well within the most sensitive limits of persons with PSE (Harding and Jeavons 1994). Other transmission mediums are likely to pose minimal risk to photosensitive individuals. Newer technology computer / VDU screens flash at a frequency of 70 Hertz without interlace which is generally considered too high to be epileptogenic. The flicker from arcade game screens is likewise too high to cause problems and handheld games employ displays that do not flicker. However, all transmission mediums will become epileptogenic if technology is introduced which contains flashing material (especially between 10-30 Hertz).

### 3.2.3 Video-game seizures and photosensitivity

Photosensitivity was positively identified during intermittent photic stimulation (IPS) on the EEG in 53% (113/213) of documented video-game seizure cases [refer to Appendix 1]. IPS failed to elicit evidence of photosensitivity in 45% (96/213) of cases and in 2% of cases this was either not tested or the results unreported.

The demographic and clinical features of the 113 VGS cases with photosensitivity appear typical for a PSE population, ie similar age of onset, seizure type. The one contrasting feature is that the majority of

video-game seizure cases have been found to be male whereas PSE populations are predominately female. This trend is probably a reflection of the gender differences in playing habits (Maeda 1990).

#### 3.2.4 Pattern-sensitive epilepsy

Individuals with pattern sensitive epilepsy can have their seizures triggered by stimuli such as escalator steps, striped material and windscreen wipers (Harding and Jeavons 1994). It appears that pattern sensitivity and photosensitivity are closely related conditions, with between 16-70% of PSE individuals demonstrating pattern sensitivity (Naquet et al 1976, Porter et al 1985, Binnie et al 1989). Although pattern sensitivity is not generally thought to occur in individuals who are not sensitive to flash (Binnie 1998) some investigators have identified occasional patients who are independently pattern sensitive (Matricardi 1990). In the largest such study, Brincotti et al (1994) found that 11/74 (16%) children with a history of visually-induced seizures were pattern but not flash sensitive. However, the presence of some special features in the sample, 39% were mentally retarded and 27% had neurological abnormalities, limits generalisation of these findings.

#### 3.2.5 Video games and pattern sequences

Video-game material will often contain geometric patterns, such as a moving checkered background or oscillating bars that can be highly epileptogenic, especially if they are repetitive.

### 3.2.6 Video-game seizures and pattern sensitivity

Pattern sensitivity was positively identified during testing in only fourteen of the 213 cases reported in the literature. However, it appears that in more than 90% of the documented cases, pattern sensitivity testing was not undertaken or the results were unreported. Only four of the fourteen tested cases were sensitive to pattern without being sensitive to flash sensitivity. All four cases were identified by a single test centre [refer to Appendix 1].

### 3.3 Other possible explanations

(ii) In the remaining 45% of documented cases the nature of the link between video game and seizure remains **uncertain**.

For this group, four possible explanations appear appropriate:-

#### 3.3.1 Inadequate testing for visual factors

Some investigators have suggested that inadequacies in both the technical and procedural aspects of visual sensitivity testing may lead to a 'false negative' result in photosensitive persons (Harding and Jeavons 1994). Factors which may affect the sensitivity of testing are listed in Table 1 (adapted from Harding and Jeavons 1994).



Table 1 Test factors open to variation between centres

Type of photostimulator	Use of diffuser / grid
Range of flash frequency	Testing with eyes open / closed / closure
Duration of stimulation	Background illumination
Intensity of stimulation	Distance of lamp from subject

Despite the scope for variation, a comparison of the results from two epidemiological studies of PS suggest that 'false negatives' are likely to be uncommon. Quirk et al (1995) conducted a survey of virtually all incident cases of PSE in Great Britain over two three month periods. No attempt was made to standardise the IPS test methodology in the 118 participating EEG departments. In a cross-sectional study, Kasteleijn-Nolst Trenite (1989) identified PSE cases attending a single test centre in the Netherlands devoted exclusively to the treatment of epilepsy. An IPS test methodology aimed at maximising detection rates was employed. Both of these studies reported similar rates of affected individuals (10% and 8% of children and adolescents respectively), which suggests that variations in test methodologies does not crucially affect sensitivity rates, particularly in unmedicated, presenting cases.

### 3.3.2 A new type of reflex epilepsy?

#### Other reflex mechanisms of potential relevance to VGS

Previous studies in the general reflex epilepsy literature have reported isolated yet verified cases of seizures associated with bodily movement, game-playing, thinking, startle and listening to music which could conceivably play a role in the genesis of some video-game seizures.

##### 3.3.2.1 Game-playing epilepsy (GPE)

Epileptic seizures precipitated by game-playing have been described previously, but appear to be rare. Ch'en et al (1965) reported four patients who experienced generalised seizures, two of which were preceded by myoclonic jerks, whilst playing or watching card games or chess. EEG abnormalities were found to worsen during card games or chess in two of the four subjects. The author considered stress a possible trigger, observing that patients had seizures after protracted intervals of intense game playing. Forster et al (1975) reported that a twenty year old airman experienced myoclonic jerks when playing cards and chess. A resting EEG showed 3 Hz spike and wave and a chess playing seizure was witnessed during the recording. A striking and repetitive increase in the frequency of game playing seizures was noted when the subject was sleep deprived, when alcohol had been consumed and when food intake was inadequate.

Cirignotti et al (1980) reported a 26 year old male who experienced absences associated with upper limb jerking, which he described as 'arrests of thought', whilst playing cards and draughts. The background EEG consisted

of 3 Hz generalised spike and wave which increased in frequency during game playing. The author ruled out the associated stress as a contributing factor, as other agnostic situations did not affect the subject's seizure frequency, but implicated strategic decision making as a possible triggering factor.

Senanayake et al (1987) described three cases where seizures were precipitated by card games, draughts and an Indian board game called 'Punchi'. All experienced myoclonic jerks with one occasionally secondary generalising. The basic EEG was suggestive of primary generalised epilepsy with 3 Hz generalised spike and wave activity. Epileptiform activity during game playing increased substantially in one subject, showed minor increases in a second and no change in the third subject.

Goossens et al (1990) added a further 7 cases to the GPE literature. 6/7 suffered myoclonic jerks with all experiencing generalised tonic-clonic convulsions. 4/7 displayed generalised spike, spike-wave or poly-spike-wave discharges during rest or hyperventilation on the EEG. Precipitants were card games in 7/7 and Chess in 3/7. Epileptiform activity was significantly higher during activation by game-playing compared with relaxation or other tests requiring attention and concentration. It was felt that stress and long periods of play were additional activating components often needed to elicit clinical symptoms. Siegal et al (1992) report on a 25 year old female who had a documented history of seizures playing checkers. They measured generalised epileptiform activity during each task and intervals of checkers playing in order to identify potential triggering factors. An increase in epileptiform activity was noted during periods of strategic thinking ie 'considering a sequence of moves based on evaluating the consequences of previous moves',

only. Other suggested triggering factors such as attention, stress and spatial processing were not found to be strong activators of epileptiform activity.

### 3.3.2.2 Thinking epilepsy

Ingvar (1962) coined the term “epilepsia arithmetica” to describe a 19 year old girl whose seizures were regularly triggered by attempting mathematical problems. Wilkins et al (1982) described a 45 year old male with generalised convulsions reliably precipitated by mental activity. EEG recordings demonstrated bursts of generalised 2.5 Hz spike and wave complexes only during periods of mental effort. Tasks involving multiplication and division were found to be more epileptogenic than addition or subtraction. The subject demonstrated higher levels of paroxysmal activity during tasks that required greater effort. Anderson et al (1986) reported the case of a 34 year old woman who had a history of seizures precipitated by mental arithmetic. Her nocturnal EEG consisted of generalised 3Hz spike and wave activity. Daytime epileptiform activity was only present during complicated mental calculations, however it was noted that activation of epileptiform activity did not occur consistently, even during difficult mathematical problems. In one of the very few studies to systematically test the effects of thinking on epileptiform activity on an unselected population, Wiebers et al (1979) reported that only one patient from 100,000 standard EEG recordings at the Mayo Clinic between 1951 and 1979 demonstrated changes in epileptiform activity during periods of mathematical calculation.

Given that most patients with game-playing epilepsy also experience seizures during tasks that involve general thinking, it has been concluded, as might be expected intuitively, that similar mechanisms are involved.

Video-game play involves many factors that have been found to epileptogenic in subjects with both general game-playing and thinking epilepsy. These include, most notably, strategic thinking, decision-making with incalculable outcome and a 'struggle to win'. Video-game play will often continue for hours in one session and thus the length of engagement also requires consideration as a potential risk factor. It is likely that individuals who demonstrate a susceptibility to seizures when exposed to these factors in general situations could also be at risk if such exposure occurs within the context of video-game play.

#### 3.3.2.3 Startle epilepsy

Startle epilepsy is the second commonest reflex epilepsy and like game-playing and thinking epilepsy appears to affect a small but relatively homogeneous proportion of epilepsy sufferers. Alajouanine and Gastaut (1955) first reported and defined a condition in children and adolescents 'where seizures were precipitated by unexpected and sudden stimuli'. In one of the larger published series, Aguglia et al (1984) described 16 cases of 'startle epilepsy' in detail. Eliciting stimuli were acoustic in all patients and adjunctive triggers included tactile and / or proprioceptive stimuli (eg sudden brushing over skin, sudden movement) on the paretic limbs. Other common features included evidence of brain damage in 15/16 and 'dilatation of the interhemispheric fissure' revealed in 6/10 who underwent CT-scans. 'Startle' seizures in 87.5% of subjects were characterised by a 'tonic spasm' during which vertex spikes were most commonly recorded on the EEG. However, in contrast to most of the earlier reports, a number of more recent studies

suggest that startle provoked epileptic seizures are a transient phenomenon in some patients without any associated fixed deficit (Manford et al 1996).

#### 3.3.2.4 Musicogenic epilepsy

Musicogenic epilepsy appears to be a rare condition that was first recognised as a unique entity in 1937 by Critchley. Published reports, most of which document only a single case or a few subjects, have presented both interesting and unusual findings. Brens et al (1984) reported on a patient whose seizures were triggered by singing voices. It was felt that the seizures were associated with songs that contained voices with a throaty, 'metallic' quality. A further single case study (Sutherling et al 1980) reported on a 67 year old male organist who experienced stereotyped focal seizures, involving the neck and jaw, when he played a specific hymn on the organ. Jallon et al (1989) documented two further cases. Firstly, a gendarme in whom 50% of daytime complex partial seizures were musicogenic. Different types of music were implicated but those that provoked the greatest emotional response in the subject, like La Marseillaise, were found to have the greatest activating effect. The onset of his seizures was preceded by a severe head injury and EEG studies showed left temporal lobe abnormalities. In the second patient, it was found that degree of attention paid to music was a determinant of seizures, sometimes it even sufficed just to think about a type of music. An EEG recording during the Bee Gees 'Too Much Heaven' triggered off a seizure in the laboratory which was of temporal lobe origin. In the most comprehensive study of musicogenic epilepsy to date, Wieser et al (1992) reported findings of 83 sufferers (7 new cases and 76 cases previously reported in the literature). In 78% of subjects music was the only identified

seizure precipitant and in 17% of cases no spontaneous seizures had been observed. Various characteristics of the musical stimulus were found to be significant in a number of patients, including musical category, familiarity and instruments. The authors also indicated that the 'emotional reaction' to music may be implicated and that this phenomenon was frequently linked to individuals with temporal lobe epilepsy, particularly right-sided.

It appears that certain video-game seizures could be precipitated, via reflex mechanisms, by the strategy or thought associated with play. Startle aspects associated with play or the accompanying music could also be implicated. However, no previously documented video-game seizure involving non-visually sensitive individuals has been reliably linked to any of these factors. This is not entirely unexpected as some reports suggest that non-visual reflex epilepsy / seizures are extremely rare, affecting far fewer than 1% of the general epilepsy population (Roger et al 1989). However, this group of epilepsies are likely to be under-diagnosed as they are not routinely screened for in clinical practice (Zifkin and Andermann 1998).

### 3.3.3 Other aspects implicated in the genesis of video-game seizures

Certain factors eg emotional stressors, cognitive engagement, physical exertion and prior sleep deprivation have been linked to a number of seizures associated with video-game play (Ferrie et al 1994, Graf et al 1994, Binnie et al 1994). They have not only been implicated as contributing to the genesis of

video-game seizures in individuals who demonstrate visual sensitivity (VS) but also as potential independent risk factors in those who do not. These states have been previously implicated in the occurrence of first as well as habitual seizures (Currie et al 1971, Lai and Trimble 1997). They have been reported under the ~~auspicious~~<sup>auspices</sup> of generic risk factors for seizure occurrence, quite outside the context of the spectrum of the reflex epilepsies, as it has been suggested that they can promote the occurrence of seizures among a broad proportion of the epilepsy population.

Lennox (1946) gave a plausible theoretical explanation for the operation of these factors in his Reservoir Theory. He described the genesis of seizures metaphorically in terms of a filling reservoir. Psychological and metabolic stressors combine to raise the water level until a point is reached where the reservoir is full, analogous to a seizure threshold, which when exceeded will lead to an overflow of the reservoir, at which point a seizure will result.

The following section will review the empirical research which has linked these factors in general to an altered susceptibility to seizures. Studies which linked these factors specifically to the genesis of video-game seizures will be reviewed in the discussion.

#### 3.3.3.1 Emotional stressors

Stress has been defined, in general terms, as 'a particular relationship between the person and the environment that is appraised by the person as taxing and exceeding his or her resources and endangering his or her well-being' (Lazarus and Folkman 1984).

A number of studies have attempted to investigate the stress / seizure link under controlled conditions during EEG monitoring. Barker et al (1950) described 6 epilepsy sufferers who exhibited "abnormal" brainwaves during



recall of significant stressful aspects of their life experience. Stevens (1959) subjected 30 epilepsy patients to an individualised stressful interview which included directed questions, criticisms and accusations during EEG recordings. 11/30 demonstrated "abnormal" responses not seen during the routine EEG. An earlier attempt to administer a standardised interview did not elicit any previously unseen abnormalities on the EEG. Feldman and Paul (1976) described 5 patients who had a history of emotional stressors increasing their seizure frequency. All subjects went on to experience seizures under laboratory conditions when exposed to stressful video and audio recordings of 'specific problematic social interactions'. Stores (1984) performed prolonged ambulatory EEG monitoring in 28 children with absence seizures. In 5/28 an increase in seizure activity was found to be associated with documented changes in both physiological and psychological states. However, in a substantial review of the stress / seizure literature, Lai and Trimble (1997) state that there are several inherent problems in the quantification of this link. Firstly, that emotional stressors may not activate seizures directly but facilitate hyperventilation and sleep deprivation which will in turn reduce the threshold in patients. Secondly, seizures themselves can cause stress; patients may actually confuse peri or post- ictal agitation with a pre-ictal phenomenon. A further persisting problem is the lack of a universal working definition of stress. Each study appears to have a different interpretation of what a stressor should represent. Patients themselves are also likely to differ in how they interpret a stressor.

### 3.3.3.2 Cognitive engagement

Vidart and Geier (1968) made 19 EEG recordings of individuals with epilepsy whilst at work. They found two groups:- (i) those individuals where the type of activity had no effect on the number of EEG discharges (ii) individuals where it was considered that the frequency of "diffuse spike and wave" paroxysms was influenced by the type of activity undertaken, the level of alertness and the degree of attention the subject paid to the task at hand. Guey et al (1969) submitted 30 children aged 6-20 years with a high frequency of paroxysmal discharges to a 3 hour structured study program of fixed activities. These included:- (1) Periods of inactivity (2) Drawing (3) Tests eg Weschler Intelligence Scale for Children (4) Projective Tests eg non-directive interviews (5) School exercises. In 16/30 children discharges were frequent enough to allow adequate comparison between sessions. The central finding was that absences occurred mainly during periods of inactivity or drawing (90%), rarely during IQ testing (10%) and not at all during either projective tests and non-directive interviews. Although some activities did demonstrate contrasting effects on discharge rates across the group, the broad trend was supportive of a spectrum of decreasing epileptiform activity relative to greater cognitive demands that were placed on the children. It was argued that changes in epileptiform activity were not solely due to the greater/lesser attentional demands required by the task but also the interplay of emotions which that given situation involves.

In contrast to these findings, other recent studies have failed to demonstrate a suppressive effect of cognitive engagement on epileptiform activity. Binnie et al (1987) studied 91 patients aged 8-62 with various types of epilepsy for

evidence of an interaction between cognition and EA. They found that only 1/91 demonstrated a significant overall effect of task on discharge rate. Kasteleijn-Nolst Trenite et al (1990) studied 21 children aged 7 -15 years with a frequency of epileptiform discharges of between one every 2 seconds and one in ten minutes. Testing was undertaken during continuous EEG recording and comprised of arithmetic, reading and intelligence subtests. Their significant finding was that during reading left and right hemisphere discharges were increased in comparison with the rest period but the left-sided discharges were increased to a lesser extent than those on the right. The implication being that cognitive tasks may suppress EA when they activate a region of the brain within the epileptogenic zone. The wider implications of these studies is uncertain as they have tended to use highly selected populations, usually children with frequent epileptiform activity (EA), and employed test materials that are of little relevance to everyday cognitive demands. Furthermore, the link between variations in EA and susceptibility to epileptic seizures remains highly speculative

#### 3.3.3.3 Hyperventilation / physical exertion

Voluntary hyperventilation was described as an activator of seizures some 60 years ago (Gibbs et al 1939). Clinical practice has shown that voluntary hyperventilation promotes or enhances general background and epileptiform activity. This technique is now widely employed in EEG laboratories. However, studies investigating the effect of hyperventilation on seizure occurrence have produced more equivocal findings and have tended to study highly selected populations (Miley et al 1977, Sherwin 1984).

There is only a sparse literature on the effects of physical exercise on seizure occurrence. At least two studies have reported patients with a clinical history of seizures during exercise (Ogunyemi et al 1988, Schmitt et al 1994).

However, the detailed descriptions of patients given suggests a rare form of reflex epilepsy. A small number of articles have systematically studied the effects of exercise on seizure occurrence in populations without known reflex epilepsy. Esquivel et al (1991) found that compared to rest the number of absences decreased during physical exercise and increased during voluntary hyperventilation in a comprehensive investigation of twelve subjects with childhood absence epilepsy.

Eriksen et al (1994) studied fifteen women with medically-intractable seizures who underwent one hour of aerobic exercise, twice weekly, for fifteen weeks. Self-reported seizure frequency was significantly reduced during the intervention period compared with a baseline period.

#### 3.3.3.4 Sleep deprivation and seizures

Sleep deprivation has been cited as one of the most powerful activators of seizures in most forms of epilepsy (Gastaut and Tassinari 1966).

However, empirical studies have provided only moderate support for the role of sleep deprivation in promoting or enhancing the appearance of epileptiform activity. Pratt et al (1968) selected 114 epilepsy patients whose routine EEG failed to demonstrate any epileptiform activity for a further sleep deprived EEG study. After 24-26 hours of sleep deprivation, 40% demonstrated epileptiform activity during either a waking or sleep recording. After accounting for the affects of sleep and potential sampling errors approximately 50% of the appearance was attributed to the use of sleep

deprivation. Degen and Rodin (1991) investigated 190 subjects with different forms of epilepsy over two consecutive days. Routine awake and sleep EEG's were performed on the first day and after 24 hours sleep deprivation on day two. Activation rates of epileptiform activity for patients when sleep deprived were comparable to both their baseline awake (33.6% vs 27.4%) and sleeping (53.2% and 52.6%) EEG's. Klinger et al (1991) studied 141 patients with generalised spike and wave activity out of a population of 1010 who underwent a sleep-deprived EEG. The authors found that the total count of generalised spike-wave paroxysms for all patients (corrected for time) was:- (i) 407 before sleep deprivation (ii) 852 in waking stages after sleep deprivation and (iii) 641 during sleep stages following sleep deprivation. From this, it was inferred that sleep deprivation has a genuine activating influence on the EEG and that it does not act merely by way of sleep induction.

Sleep deprivation, cognitive engagement, emotional stress and physical exercise have not been reliably linked to an increased susceptibility to seizures in the general epilepsy literature and as such their relevance to video-game seizures is uncertain. The few empirical studies conducted in the area have tended to provide mixed results. The lack of a universal definition of certain factors, ie cognitive engagement and emotional stress, presents methodological problems and makes any comparison between studies difficult. Furthermore, the interpretation of these states is likely to differ greatly between individuals ie what constitutes a stressful encounter. Certain studies appear to have used highly selected populations which limits generalisation. It has also been suggested that EEG changes under the effects of such factors

fail to provide convincing evidence of increased epileptogenicity (Lai and Trimble 1997).

#### 3.3.4 Chance association between stimulus / state and seizure

The timing of epileptic seizures for most sufferers is thought to be random. Seizures can occur at work, during exercise, whilst eating, during sleep and during any other pursuits which occupy patient's lives. The frequency of association between any one activity and seizure occurrence is, in most patients, likely to be a function of the time spent pursuing it.

Video-game play represents an increasingly common pastime for children and adolescents. In a survey of 6000 7-19 year olds in Great Britain conducted between March and June 1993 (BRMB International 1993), 82% indicated that they had played a video-game previously and their mean daily exposure was 0.7 hours. This level of exposure provides support for the idea that certain epileptic seizures associated with video-game material are likely to represent a coincidence.

#### 3.4 Establishing cause and effect with video-game seizures

Investigators seeking to examine the nature of the link between video-game and seizure in cases without visual sensitivity face a number of impediments. Firstly, the quantification of certain states that may be associated with video-game play remains extremely difficult ie physiological changes, emotional stressors, altered cognitive arousal. Secondly, as mentioned earlier, epilepsy has an intermittent symptomatology and subsequently all of the video-game seizure cases that have been identified retrospectively [Refer to Appendix One]. Retrospective studies only allow speculation of likely associations,

rather than causal assertions, as they comprise uncontrolled observations often based on distant events ie the time lag between the video-game seizure occurrence and a detailed investigation has typically been some months and on occasion years.

Further investigation of the risks posed by video-game material to non-visually sensitive epilepsy sufferers appears warranted as many patients anecdotally report that video-game material does promote seizure occurrence. The interpretation of non-visually sensitive cases has an important bearing on the formulation of accurate advice for the general epilepsy population ie establishing a definite causal link in a substantial number of cases may require alerting a broader proportion of the epilepsy population, ie not just those with visual sensitivity, of the potential risks associated with video-game play.

#### 4 Aim of the main study

Against this background, the aim of the main study is determine the relative frequency of seizures during fixed equal temporal exposure to video-game material and other common leisure pursuits in patients with chronic epilepsy without visual sensitivity. This study has been designed to:- (i) enable some evaluation of the role of certain non-photic factors implicated in previously documented video-game seizures eg sleep deprivation, arousal and prolonged exposure and (ii) identify whether some new previously unrecognised factor, ie a new type of reflex epilepsy, might be involved in some video game seizures. The results of this study may serve to determine more accurately what proportion of the general epilepsy population are at risk from video-game material.

In some preliminary work prior to and in the early stages of the main research project, two questionnaire studies (Studies 1 and 2) were undertaken in order to determine whether epilepsy sufferers have concerns about being exposed to video-game material and what sort of information they have received about the safety of video-game play and general exposure to photic material.



## 5.1 Study One

### Patient perceptions of video game material / electronic screens and other factors as seizure precipitants: a questionnaire study

A survey of epilepsy sufferers was conducted with the following aims: (i) to ascertain epilepsy-patient views regarding the risk of seizures due to video-game playing in all people with epilepsy, and (ii) to investigate the factors which individuals with epilepsy perceive to precipitate their own seizures - with a particular emphasis on those factors (sensory and non-sensory) that have been linked to video-game seizures.

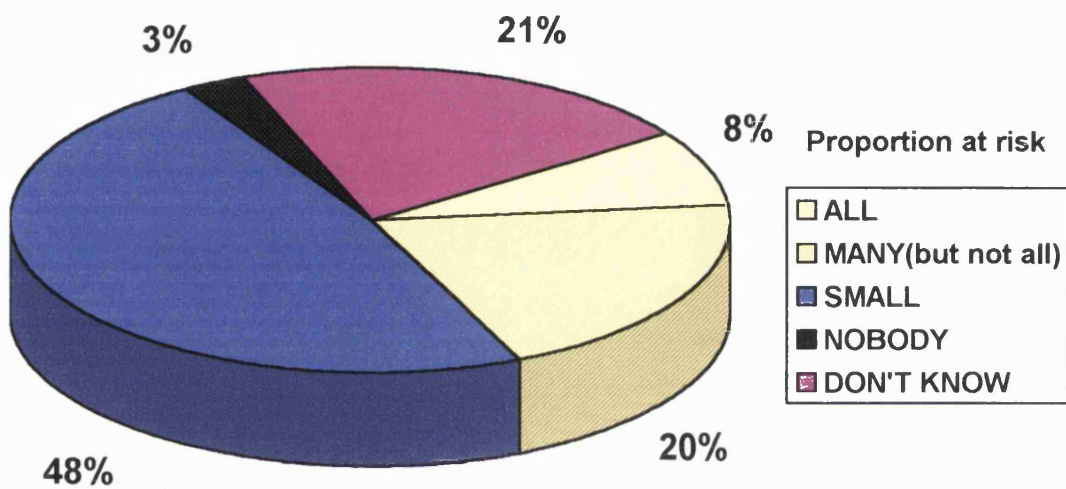
#### Method

The survey sample consisted of predominantly adult patients attending the specialised epilepsy clinics run at the Outpatients Department of the National Hospital for Neurology and Neurosurgery over a six month period (October 1995 - March 1996). To select a sample with active epilepsy, any patient who had not suffered a seizure in the six months prior to the consultation was excluded from the study. A total of 396 patients were approached to complete the survey. Thirty two (8%) of these either refused to participate or failed to complete the questionnaire to minimal standards (N=364). [See Appendix 2 for survey format]

#### Results

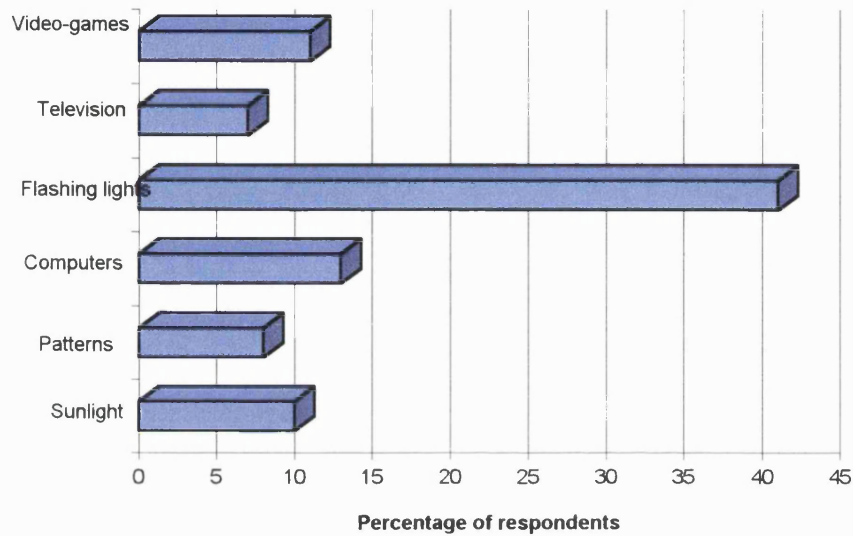
Participants were aged between 13-77 years (median 31 years). There were 182 females and 182 males.

Figure 2: Epilepsy patient perceptions of seizure risk due to video-game material in others with known epilepsy



The data demonstrate that the perceived risk of playing video-games for many epilepsy sufferers is high. More than one in four (28%) patients surveyed believed that either 'All' or 'Many' of the epilepsy population were at risk from this stimulus. Those that responded 'All' were not from a specific subpopulation, ie by gender or age. Furthermore, one in five (21%) were unaware of who was at risk when using video-game material.

Figure 3 Perceived seizure precipitants for individuals with known epilepsy



The proportion of individuals who considered video games as a precipitant of their seizures was greater than expected (10.2%), although this was not substantially different from either television (7.9%) or computer (12.6%) 'at risk' percentages. A surprisingly high proportion of participants (41%) felt that exposure to flashing lights could precipitate their seizures.

## 5.2 Study Two

### Patient recall of their IPS test result and their general concerns about being exposed to photic material: a questionnaire study

The results from the initial questionnaire suggest that exposure to video-game play and other photic material is widely interpreted as promoting an increased risk of seizures by many patients with epilepsy. The aim of this follow-up questionnaire study was to explore the nature of the information that patients recall receiving about their IPS test result as well as whether they received any advice about interacting with environmental sources of flickering and other light.

#### Methods

One hundred and thirty seven individuals with epilepsy attending a tertiary referral centre were approached and asked to participate in the study. Twenty-six patients had not undergone an EEG with IPS previously. A further eleven were excluded for other reasons; six for not filling the questionnaire in properly and five who could not recall if they had been informed of the results of the IPS procedure. The remaining one hundred participants correctly completed a short survey (see Appendix 3). Participants were at least sixteen years of age, mostly with severe intractable epilepsy and a proportion were being considered for surgical therapy due to a diagnosis of intractable partial epilepsy (mostly temporal lobe); ie a group which would be considered at an exceptionally low risk of harbouring photosensitivity-less than 5%.

## Results

### **Are you sensitive or not to IPS?**

Of the sample 12% reported being informed that they were sensitive to flashing lights, 37% reported being informed that they were not sensitive to flashing lights and the remaining 51% could not recall being informed of their test result.

### **Have you been given advice about being exposed to flashing lights?**

(a) Sixty-three per cent felt that they had not been given any advice

(b) Three per cent felt that they were given advice indicating that they were *not* at an increased risk of a seizure whilst exposed to flashing lights and / or other environmental photic stimuli

(c) Thirty-four per cent felt that they were given advice indicating that they were at an increased risk of a seizure whilst exposed to flashing lights and / or other environmental photic stimuli and they were actively encouraged to avoid such material (eg television, sunlight, discos, visual display units, video-game material)

Medical practitioners gave 76% of the advice.

### **Common examples**

'I was basically told to avoid flashing lights'

'To stay away from discos and computers'

'Told to avoid flashing lights, eg discos, strobe lights and TV interference'

'Told to avoid lights in the place of work if possible' (This participant was employed in a photography laboratory).

It appears that the IPS test result is not being relayed to all patients, at least in a way that they can understand and retain; a proportion of participants had probably been informed of their test result but had subsequently forgotten it. I also found good evidence to suggest that misinformed attitudes about the wider epilepsy populations' risk of seizures while exposed to photic material, including video games, are highly prevalent. Approximately one third of the sample appeared to be given advice aimed at restricting their exposure to material that utilises a light source.

Although the questionnaire studies are not readily generalisable and may not represent the views of all epilepsy sufferers, they do indicate that there is a considerable problem of misinformation and misunderstanding around these issues. The results obtained do further emphasise the need for the main study.

## **6 Study Three: the main study**

### **Methods**

A pilot study was conducted in the two weeks preceding the start of the main investigation (mid June 1995). 6 patients participated during this time. This was conducted to:-

- (i) determine the optimum length of individual sessions / total program for which a reasonable degree of participant interest would be maintained
- (ii) sort out any other potential problems

### **6.1 Setting**

The studies were conducted in a 6-bedded long-stay video EEG facility with an annual throughput of between 400-500 patients at a specialist neurology hospital. Patient referrals were broadly classifiable into three main diagnostic categories:- known epilepsy, blackouts of uncertain aetiology and sleep disorders. Approximately 25% of admissions to this facility were suitable for the study as their stay exceeded 24 hours and they had a definite diagnosis of epilepsy ie cases where the referring physician expressed any doubts regarding the diagnosis, no matter how slight, were not invited to participate.

The reason for referral of patients invited to participate in the study was to evaluate:-

- (i) their suitability for epilepsy surgery - the aim of the investigation was to record habitual epileptic seizures that may assist in determining whether the epilepsy was localised to a specific brain region.
- (ii) their seizure type

(iii) the efficacy of a newly introduced AED

### EEG recordings

A set of silver-silver chloride electrodes was affixed to all patients conforming to the universal 10-20 system of electrode placement. Pads for recording an electrocardiogram (ECG) were placed on the chest of each patient. Respiratory parameters were also recorded in certain patients when clinically indicated. All electrodes fed into a patient transmitter box which attached to a telemetry cable which feed into a local recording site. The length of the telemetry cable allowed the patients free movement within their room although occasionally they had to disconnect themselves and interrupt the recording ie to use the bathroom.

Each patient's EEG tracing was transmitted to the central recording room where it is recorded onto an optical disk for later review. Similarly, video recordings were made with a VHS unit. Both sets of recordings had the time displayed, which was synchronised, to enable the reviewer to accurately compare clinical and electrophysiological findings. EEG recordings could be remounted during review and all were archived on DAT tapes.

#### 6.1.1 Surveillance of patients

During the period of the study (July 1995-January 1998), active surveillance was undertaken on patients at all times during their admission.

(a) Video - video footage of each room was transmitted to three different sites on the unit. Constant monitoring took place at least one of these sites ie usually the nurses station.



(b) EEG - EEG recordings were displayed in every room constantly as well at two other sites. Computer generated seizure and spike detection programs consolidated the surveillance effort.

(c) Eyewitness - a number of staff were employed at the unit eg nurses, technicians, scientists, researchers and doctors and there was thus a constant stream of staff passing by each room who ~~to~~ could have alerted if a seizure was taking place

(d) Patient self report - each patient was given a seizure diary at the start of their admission in which they were asked to indicate any seizures (if they can recall them) or other subjective sensations. Each room contained an 'aura' button which the patient was asked to press if possible to alert the staff that they were about to have a seizure.

The level and different forms of surveillance on the telemetry unit would have made it extremely unlikely that any seizure would have gone undetected over the period of the study. Furthermore, the methods of surveillance were uniform throughout the entire study period which minimised the possibility of bias. Recorded EEG and video recordings was retrospectively reviewed by trained technical staff. Periods in which a ictal event was suspected were reviewed meticulously. Independent technical staff were used to differentiate between a clinical seizure and a non-clinical (subclinical) ictal electrographic event.

## 6.2 Subjects

Two hundred and forty seven (247) individuals with epilepsy agreed to participate in the study during their admission to the video EEG monitoring

unit between July 1995 and February 1998. This represented a participation rate of 85% of all suitable first-time admissions (278) over this period; 11 were not considered because they had known VS. Twenty either refused to partake in the study or were otherwise unavailable. The latter did not differ from participants with regards age, gender or seizure type.

#### 6.2.1 Exclusion rationale

(a) Any subject who was found to have experienced a clinical seizure in the 90 minutes preceding the scheduled start time which was only 'picked up' during a later EEG review was excluded (N1=4). This was aimed at minimising the number of patients entering the study in the middle of a cluster of seizures. In occasional subjects a clinical seizure occurred and was recognised in the 90 minute period before the scheduled start time. In these cases, rescheduling of the study to a different time or day was permitted, if this was feasible.

(b) Meal-break seizures - the length of the study program (6 hours) necessitated a break of either 45 or 60 minutes for lunch or dinner. Meal-breaks were not part of the study program and thus participants who experienced seizures during this time were therefore excluded from the study (N2 = 8)

(c) Participants whose diagnosis of epilepsy was questioned in the light of video EEG findings were excluded retrospectively (N3 = 4)

(d) Withdrawals - a number of participants withdrew from the study before it's completion due to either a lack of interest or to unforeseen social / clinical commitments (N4 = 19).

The remaining 212 subjects completed the study.

**Table 2** Participant characteristics and clinical data

Parameter	Participants (%)
Gender	100 females (47), 112 males (53)
Age	Median 31 years, Interquartile range 26-39 (Range 16-57)
IQ	No minimum requirement, although virtually all subjects > 70
Possible Aetiology	Febrile convulsion (30), Head trauma (7), Encephalitis (4), Meningitis (3), Other (4), None known (52)
Imaging Abnormalities	Focal (72) [Temporal (69), Extratemporal (3)], Generalised / Multifocal (7), Normal (17), No imaging (4)
Seizure type	Absence (5), Simple partial (37), Complex partial (91), Generalised Tonic-Clonic (42)
Seizure Frequency	≥ 1 / day (20), 1-6 / week (48), 1-4 / month (31), < 1 / month (1)
AED combination	Monotherapy (16), Two AED's (55), Three or more AED's (29)

**6.2.2 Special group features (see Appendix Four)**

**6.2.2.1 Antiepileptic drug (AED) reduction:-** 59% of the sample were on reduced levels of anticonvulsant medication at the time of their participation in the study.

**6.2.2.2 Partial sleep deprivation** was a further provocative technique employed to promote seizures in 24% of the study sample. This involved requesting that patients remain awake, with nursing supervision, until 2am. Subjects were then allowed four (4) hours sleep and were woken at 6am. A decision to sleep deprive was usually taken on the second night of the

patient's admission, if an insufficient number of seizures ( $< 2$ ) had been recorded.

AED reduction and partial sleep deprivation were undertaken in patients solely for clinical purposes.

### 6.3 Material

**Table 3 Materials**

<b>Video Game System</b>	<b>Software</b>
(1) Sega 16X (+ 32X)	The Lion King, Fifa Soccer '95, Virtuo Racing, Sonic and Knuckles, Sylvester and Tweety
(2) SuperNintendo	Wild and Wacky Sports, Tazmania, Donkey Kong Country, The Jungle Book, Earthworm Jim
(3) Sega Saturn System	Pebble Beach Golf, Ralley Racing, Virtuo Cop, Pinball, Bug, Clockwork Knight
<b>Leisure materials</b>	
24" (50 Hertz) colour television - with broadcast or recorded material, Exercise Bike, Puzzle Books, Reading Material:- Books, Magazines, Newspapers, Knitting, Radio/ Cassette / Compact Disc Player etc	

Video-game consoles were played on a 24" colour television (50 Hertz) at a distance of between 0.8 and 1.4 metres. The selection of video-games was purposefully based on what was popular on the market at the time of the study in order to relate to the commoner situations in the community.

#### 6.4 Procedure

All patients with definite epilepsy staying > 24 hours on the telemetry unit underwent a detailed clinical assessment and a comprehensive evaluation of their seizure disorder. Each subject was then rigorously tested for flash and pattern sensitivity according to currently recommended protocols (Harding and Jeavons 1994); refer Appendix Five. This was a routine provocative procedure for all admissions. Eleven patients, representing 4.3% of the eligible population, were found to be photosensitive; most cases (9/11) were not newly diagnosed but had demonstrated Type 4 photosensitive response (Waltz et al 1993) on a previous EEG investigation. These patients did not partake in the study. The proportion of cases that were found to be photosensitive was within the expected range.

Suitable patients without visual sensitivity were then approached and informed about the nature and purpose of the study. A number of the important practical details were also discussed eg the amount of time commitment required, the need for strictly controlled experimental conditions. Each patient was then asked to preliminary indicate whether they felt they would like to take part. Twenty individuals were either not willing to participate in the study or were otherwise unavailable. Patients who agreed in principal to participate were asked to help to decide which day of their admission would be most suitable. This decision needed to take into account the timing of the patient's clinical commitments, eg psychometric testing, psychiatric assessment, imaging studies, as well as social engagements, eg visits from relatives and friends. The day selected was therefore essentially random.

On the proposed study day, all subjects were asked confirm that they would still like to participate. Before the commencement of the study, each subject was then randomly allocated (see Appendix Six for random allocation procedure) to a first period of either video-game play or other leisure activity by use of a sealed envelope. Separate series of envelopes were prepared for each day of the week as well as for single patients or for pairs (these were chosen accordingly as one or two participants were to be randomised on the same day. The pairs allocated one patient to each activity in the initial period). Within each strata the envelopes were kept and opened in strictly increasing order of their serial numbers.

After completing the first period of video-game play or other leisure for 45 minutes subjects then alternated between these activities for a further seven study sessions each of 45 minutes duration (8 x 45 minutes in total).



**Table 4 - A typical study timetable**

<b>WEDNESDAY 1</b>		
09:00-09:45	<b>Video Game Activity</b>	<b>Session 1</b>
09:45-10:30	<b>Alternative Leisure</b>	<b>Session 2</b>
10:30-11:15	<b>Video Game Activity</b>	<b>Session 3</b>
11:15-12:00	<b>Alternative Leisure</b>	<b>Session 4</b>
12:00-13:00	<b>MEAL BREAK</b>	
13:00-13:45	<b>Video Game Activity</b>	<b>Session 5</b>
13:45-14:30	<b>Alternative Leisure</b>	<b>Session 6</b>
14:30-15:15	<b>Video Game Activity</b>	<b>Session 7</b>
15:15-16:00	<b>Alternative Leisure</b>	<b>Session 8</b>
16:00	<b>END OF STUDY</b>	

**Table 5** Study days and times

Tuesday	13:30 - 18:00	(6 x 45 minute sessions)
	18:00 - 18:45	Dinner Break
	18:45 - 20:15	(2 x 45 minute sessions)
Wednesday	09:00 - 12:00	(4 x 45 minute sessions)
	12:00 - 13:00	Lunch Break
	13:00 - 16:00	(4 x 45 minute sessions)
Thursday	09:00 - 12:00	(4 x 45 minute sessions)
	12:00 - 13:00	Lunch Break
	13:00 - 16:00	(4 x 45 minute sessions)

Participants were allowed a 60 minute break for lunch on the Wednesday and Thursday sessions. The Tuesday program started and concluded later than the other days, as this fitted in better with the ward routine, and the break for dinner was restricted to 45 minutes.

I personally oversaw all of the studies and ensured that every effort was made to adhere to the designated times. However, occasional deviations from these were inevitable.

#### 6.4.1 Deviations from the timetable

Occasional deviations from the timetable were due to:-

- (a) A late start to Session One Lunch and dinner was served promptly at fixed times in the day. In occasional studies, where a late start was unavoidable, it was necessary to reduce the time of two or four sessions by up to five minutes so that the morning or afternoon block (depending on the day) would be completed in time to finish for the meal break. Any reduction in the time was done equally to video-game and leisure sessions so that the net effect was always an equal total gross time exposure (~ 3 hours) to both types of sessions for each participant.
- (b) Toilet breaks Session timings were altered slightly to ensure that there was approximately equal total time exposure to video-game and leisure sessions over the program for each subject.
- (c) Technical difficulties - very occasionally, technical difficulties would arise with video-game material, any time lost would be dealt in same way as (b).

The total alterations to the timetable for the reasons stated above were extremely minimal, with the majority of participants having 8 full sessions of 45 minutes each.

#### 6.4.2 Video-game sessions

Subjects were provided with the most recently released video game systems and were provided with 5 or 6 games to choose from (see Materials section). Participants were encouraged to play a different game in each of their four

video game sessions, giving them an opportunity to be exposed to various types of game content and strategy. However, to maintain maximum interest they were allowed to change to a different game during a session or play a single game in a number of sessions. Subjects sat in a comfortable chair during VG play at a distance of between 0.8 and 1.4 metres from the screen. Participants who were unfamiliar with the particular games console or video games in general were given a brief explanation of how the each game worked to encourage enjoyment and discourage non-compliance.

#### 6.4.3 Alternative leisure sessions

Subjects were allowed to choose what to do during their leisure sessions. They were encouraged to do a variety of activities such as word puzzles, reading, physical exercise, listening to music, playing cards or chess / draughts, quiet rest or any other activities that were appropriate given the space and time limitations. Subjects were permitted to change between leisure activities mid-session if they so desired.

The study ceased if the participant experienced a clinical seizure.

#### 6.4.4 Measurement

(i) Only clinically apparent seizures were included in our final analysis. A number of independent technical staff were used to differentiate between a clinical and non-clinical (purely electrographic) seizures.

Information recorded for all clinical seizures included:-

- (a) Seizure type eg simple partial, complex partial, primary/secondary generalised tonic-clonic
- (b) Seizure semiology eg description of clinical features eg shouting, dystonia, automatisms, stiffening
- (c) EEG features
- (d) ECG changes immediately preceding and during the seizure
- (e) Session Number (1-8)
- (e) Activity of that session (VG or L)
- (f) If VG, following was recorded:- type of system, which game, level of difficulty, subjective rating of excitement of participant, time in session
- (g) If L, following was recorded:- type of activity, time in session

#### 6.4.5 Video Game Seizure Subjects

- (i) Were asked to confirm that they had no history of video game or other photic-induced seizures.
  
- (ii) Were asked whether they could recall experiencing any visual disturbance as part of the seizure.
  
- (iii) Were asked, to their knowledge, whether the video game seizure was any different to their habitual seizures (this was also investigated by comparing features if the subject experienced other seizures during their stay on Telemetry or compared with their detailed seizure description obtained from the medical notes).

#### 6.4.7 Statistical Analysis

Patients entering the study (except for withdrawals / exclusions) could only have had one of three possible outcomes:- (i) they completed the study seizure free (ii) they terminated the study with a seizure during an alternative leisure session (iii) they terminated the study with a seizure whilst playing video games. This gives rise to a multinomial (strictly trinomial) distribution of outcome as shown below.

#### Outcome

<u>Seizure-free</u>	<u>Seizure during leisure</u>	<u>Seizure during video game</u>	<u>Total</u>
$n$	$n_L$	$n_{VG}$	$N$

where  $n + n_L + n_{VG} = N$

The proportion of patients having a seizure during leisure (video games) is estimated simply by  $n_L / N$  ( $n_{VG} / N$ )

with variance  $n_L (n + n_{VG}) / N^3$  [ $n_{VG} (n + n_L) / N^3$ ]

The variance of the difference between these proportions

$(n_{VG}/N - n_L/N)$  is estimated by:-

$(n_{VG} + n_L) n + 4n_{VG} n_L / N^3$

The 95% confidence interval for the difference between these proportions is obtained by subtracting and adding

$$1.96 \sqrt{(n_{VG} + n_L)n + 4n_{VG} n_L / N^3} \quad \text{to this difference.}$$

### The Weibull Model

The Weibull Model is a parametric survival model which allows incorporation of changing risks ie risks which change over time. In the present study I was interested to see whether or not the risk of a seizure increases with time; which may represent a fatigue effect or loss of arousal. The Weibull model has two independent parameters,  $\lambda$  and  $\delta$ , and takes the following form for the hazard function:-

$$\lambda(t) = \lambda \delta \cdot t^{\delta-1}$$

Gross and Clarke (1975) refer to  $\lambda$  as the scale parameter and to  $\delta$  as the shape parameter. The Weibull hazard function increases, remains constant, or decreases according to whether  $\delta > 1$ ,  $\delta = 1$  (ie exponential), or  $\delta < 1$  respectively. Interestingly Parmar and Machin (1995) just refer to the "two-parameter Weibull model" and do not use the terms "scale" and "shape". The Weibull model (and others) can be formulated as a log-linear model which fall within a general class of accelerated failure time models (AFT models). AFT models incorporate a constant or intercept parameter and a scale parameter denoted by  $\sigma$ . The scale parameter  $\sigma$  in the accelerated failure-time model is the reciprocal of the shape parameter,  $\delta$ , in the Weibull hazard model. The confusion arises from the different model formulations plus use of the terms "shape" and "scale" in the two contexts.

## 7 Results of the main study

### 7.1 Summary of main finding

25/212 subjects experienced clinical seizures during the study program.

Thirteen experienced seizures during sessions of video game play and twelve experienced seizures during sessions of alternative leisure [doing word puzzles (n=2), engaged in conversation (n=3), reading (n=3), watching television (n=2), writing a letter (n=1) and listening to music (n=1)].

### 7.2 Detailed description of cases

#### Study seizures during:-

##### Video Game Play

**VGS1** A 35 year old man with a 9 year history of epilepsy following a frontal craniotomy for a pituitary adenoma reported no family history of epilepsy. His seizure frequency was estimated to be one per fortnight. During telemetry, his interictal EEG showed a clear cut right frontal epileptiform foci. The seizure pattern was of (i) frequent mainly subclinical right frontal seizures and (ii) non-localising/lateralising clinical seizures, all of which involved the need to vomit, one of which involved jerking of the right arm and generalisation. MRI findings were consistent with right mesial temporal lobe sclerosis. There was also a high signal change at the right frontal pole. PET studies showed changes in the right frontal lobe and an asymmetry in the temporal lobes. His daily medication on admission was Phenytoin 1125mg, Carbamazepine 1000mg and Sodium Valporate 1400mg. Drug reduction was instituted. The video-game seizure occurred at 15:01, thirty seconds into session three. The subject was playing the SuperNintendo system. This seizure was electroclinically similar to other seizures experienced on the unit and the patient described it as habitual.

**VGS2** A 32 year old male with an onset of seizures aged 22 possibly related to head injuries sustained from a motorbike accident one year earlier. There was no reported family history of epilepsy and seizure frequency was estimated to be 8 per week. During telemetry, his interictal EEG showed infrequent sharp waves over the left temporal region but also more widespread and bilateral abnormalities. The ictal EEG consisted of widespread slow activity over the left hemisphere during frequent subclinical and clinical attacks. The clinical features were compatible with temporal lobe epilepsy (TLE) probably in the dominant hemisphere (speech disturbance). MRI was reported as normal. His medication on admission was Carbamazepine 800mg and Lamotrogine 300mg. Drug reduction was not instituted. The video-game seizure occurred at 16:42, 42 minutes into session 4. The subject was playing the Sega 32X system. This seizure was electroclinically similar to his other documented events.



**VGS3** A 23 year female with a 16 year history of seizures of unknown aetiology with no reported family history of epilepsy had previously undergone a left temporal lobectomy. Her seizure frequency was estimated to be several per day. During telemetry, her interictal EEG was characterised by frequent spikes in the left posterior temporal/parietal region which were more generalised during sleep. The subject's seizures consisted of:- (i) non-localising left hemisphere clinical features (right-handed dystonia) (ii) EEG features suggestive of a posterior onset (posterior temporal/parieto-occipital) which were either left sided or bilateral. MRI findings showed evidence of a limited left temporal lobectomy with a subdural haematoma related to this. Her medication on admission was Carbamazepine 1400mg and Lamotrogine 150mg. Drug reduction was not instituted. The video-game seizure occurred at 14:17, 32 minutes into session 6. The subject was playing the SuperNintendo system. This seizure had similar electrographic and clinical features (including eye/head deviation to the left and right-handed dystonia) to six other documented seizures during her five day admission.

**VGS4** A 29 year old female experienced a febrile convulsion in childhood but there was no other significant neurological/family history. She experienced approximately 8 seizures a month. During telemetry, her interictal EEG showed very frequent left temporal spiking. The documented seizures were:- (i) clinically suggestive of left TLE (grimacing, right-handed dystonia) and (ii) electrographically left sided, although covering a wide field. MRI findings were suggestive of left hippocampal sclerosis. The subject's medication on admission was Carbamazepine 1200mg, Lamotrogine 150mg and Clobazam 40mg. Drug reduction was instituted. The seizure occurred at 19:44 which was 14 minutes into session eight. The subject was playing the SuperNintendo system. The video-game seizure was electroclinically similar to 11 other documented seizures during the subject's five day admission.

**VGS5** An 18 year old male with seizures since the age of 12 had no family history of epilepsy. His seizure frequency was approximately 5 each week. During telemetry recordings, his interictal EEG showed no epileptiform activity. The 2 documented seizures were reported:- (i) electrographically as having repetitive sharp and slow wave transients over the right parietal lobe (ii) clinically as consisting of clonic movements in the left hand and side of face. MRI findings were of a solitary mass in the right perirolandic region of the middle frontal gyrus suggestive of a (DNET) or low grade glioma. His medication on admission was Phenytoin 300mg, Sodium Valporate 800mg and Carbamazepine 800mg. Drug reduction was not instituted. The video game playing seizure occurred at 13:58, 8 minutes into session 6, whilst the subject was playing on the SuperNintendo system. This seizure was electroclinically similar to one other experienced during the patient's stay on the unit.

**VGS6** A 33 year old female had no family history of epilepsy or other recognised aetiology. Her seizure frequency was estimated to be 4 each week. During telemetry recordings her interictal EEG showed left temporal spikes with a wide distribution. The recorded seizures showed:- (i) a left temporal rhythmic discharge electrographically (in one attack) and (ii) left temporal lobe features (right-handed dystonia) clinically. MRI findings were suggestive of left mesial temporal sclerosis. Her medication on admission was Sodium Valporate 400mg and Carbamazepine 800mg. Drug reduction partial sleep deprivation were instituted. The video-game playing seizure occurred at 16:29, 19 minutes into session 8. The subject was playing the SuperNintendo system. The video-game seizure was clinically but not electrographically similar to another spontaneous seizure witnessed during the subjects stay on the unit.

**VGS7** A 37 year old male with a thirty year history of epilepsy reported they he suffered several febrile convulsions between the ages of 2 and 5. He estimated that his seizure frequency was 3 per month. During telemetry, his interictal EEG was unremarkable during the day but showed sharp waves, spikes and polyspikes with maximum amplitude at F8. He suffered

several non-epileptic seizures during his admission which was compatible with his known clinical history. He also experienced four definite epileptic seizures, none of which provided information of the focus of his seizures. MRI studies supported a diagnosis of right hippocampal sclerosis. His medication on admission was Carbamazepine 1600mg and Gabapentin 1800mg. Drug reduction was instituted. The video-game playing seizure occurred at 14:30, 15 minutes into session 4, whilst playing the Sega Saturn system. The video-game seizure was electroclinically similar to two other documented seizures experienced during his admission.

**VGS8** A 40 female suffered a severe head injury aged 13 months and had a 37 year history of habitual seizures. She estimated that her seizure frequency was 4-6 a week. During telemetry, her interictal and ictal EEG features were supportive of right temporal lobe epilepsy. MRI studies confirmed right hippocampal sclerosis. Her medication on admission was Carbamazepine 500mg, Clobazam 50mg and Topiramate 50mg. Drug reduction was instituted. The video-game playing seizure occurred at 13:55, 5 minutes into session 6, whilst playing the Sega Saturn system. It was clinically similar to 5 other seizures experienced during her admission. No ictal EEG was available.

**VGS9** A 57 year old male suffered an encephalitic illness aged 4 and suffered habitual seizures since, despite a recent partial right temporal lobectomy. He suffered up to 3 seizures daily. During telemetry, his interictal EEG demonstrated frequent spike and wave discharges in the right fronto-temporal regions. The EEG during his three recorded seizures was stereotypically right frontal and then gradually began right temporal. MRI studies noted a previous minor right temporal lobectomy with some residual atrophy of the right hippocampus. His medication on admission was Carbamazepine 1600mg, Clonazepam 8 mg and Topiramate 300mg. Drug reduction was instituted. The video-game playing seizure occurred at 19:55, 23 minutes into session 8 whilst playing the Sega Saturn System. It was electroclinically similar to the other two seizures experienced during his admission.

**VGS10** A 28 year old male suffered a febrile convulsion aged 3. He began to experience habitual seizures from age 6 years. He estimated his seizure frequency to be 2 per month. During telemetry, his waking interictal EEG demonstrated rare left temporal spikes. The three seizures suffered during his admission were clinically compatible with left TLE. The EEG features were somewhat equivocal but favoured a left sided onset over a wide field. MRI investigations showed features consistent with left hippocampal sclerosis. His medication on admission was Carbamazepine 2000mg and Topiramate 200mg. Drug reduction and partial sleep deprivation were instituted. The video-game playing seizure occurred at 12:07, 37 minutes into session 4, whilst playing the Sega Saturn console. It was electroclinically similar to two other seizures suffered during the admission and the patient described it as habitual.

**VGS11** A 38 year old male with a family history of epilepsy estimated his seizure frequency to be between 6-8 per month. The telemetry recordings, both interictal and ictal, were supportive of right temporal lobe epilepsy. An MRI study suggested right hippocampal sclerosis. His medication on admission was Primidone 1000mg. Drug reduction was not instituted but the patient was sleep deprived on the night preceding the study. The video-game playing seizure occurred at 15:14, 44 minutes into session 7 whilst playing on the Sega Saturn system. The patient did not suffer any other seizures during his admission for comparison, but he described it as habitual.

**VGS12** A 26 year old female with no known aetiology reported experiencing up to 7 seizures a day. During telemetry, her interictal EEG showed occasional right temporal spikes. Her ictal EEG was difficult to interpret, as it was frequently obscured by muscle artefact, but involved

both temporal lobes at different stages of the seizure. MRI studies showed an area of localised parenchymal damage in the frontal and temporal lobes as well as a widespread atrophy in the right frontal lobe. Her medication on admission was Carbamazepine 1600mg and Gabapentin 1600mg. Drug reduction was instituted during her admission but normal medications were resumed at 8pm on the night preceding the study. The video-game seizure occurred at 15:01, 28 minutes into session 7, whilst playing on the Sega Saturn console. The patient suffered 5 other seizures during her admission and all very fairly stereotyped.

**VGS13** A 50 year old male reported suffering a severe head injury aged 9 months and also had an extensive family history of epilepsy. He suffered nocturnal seizures from 9 months until his early 30's but more recently he described suffering several day and night seizures a week. During telemetry, his EEG recording showed right temporal region sharp waves interictally. The ictal EEG had little localising value as the first EEG changes occurred more than 30 seconds after the initial clinical onset. MRI investigations demonstrated left hippocampal sclerosis. His medication on admission was Lamotrigine 400mg, Phenobarbitone 30mg and Phenytoin 1500mg. Drug reduction was instituted. The video-game seizure occurred at 13:40, 10 minutes into session 1, whilst playing the Sega Saturn system. The study period seizure was electroclinically similar to two others suffered by the patient during his admission.

### **Alternative Leisure Sessions**

**LS1** A 20 year old female had a history of epilepsy from age . She experienced febrile convulsion in childhood but reported no family history of epilepsy. Her seizure frequency was estimated to be 6-8 per week. During telemetry, her interictal EEG showed frequent epileptiform activity over the left temporal region. The ictal EEG and clinical features of all three complex partial seizures documented were compatible with left TLE (right-handed dystonia). MRI findings were of an abnormal appearance of the left hippocampus typical for hippocampal sclerosis as well as an extra-hippocampal abnormality in the left temporal lobe white matter. Her daily medication on admission was Sodium Valporate 800mg and Carbamazepine 1400mg. Drug reduction was instituted. The leisure activity seizure occurred at 13:55, 10 minutes into session 6, whilst doing word puzzles. This seizure was electroclinically similar to other seizures experienced on the unit and the patient described it as habitual.

**LS2** A 30 year old male with a year history of seizures reported no family history of epilepsy. His seizure frequency was estimated to be two per day. During telemetry, his interictal EEG consisted of infrequent sharp waves over both hemispheres. The subject's seizures consisted of:- (i) clinical features compatible with TLE but non-lateralising (swallowing, eye blinking and jaw movements) and (ii) EEG epileptiform activity arising from the left temporal region. MRI findings were suggestive of a low grade tumour in the left hemisphere, concentrated in the temporal lobe. His medication on admission was Carbamazepine 1200mg and Clonazepam 2mg. Drug reduction and partial sleep deprivation were instituted. Sleep deprivation was carried out on the night preceding the study; the subject was allowed 4 hours sleep from 2am to 6am. The leisure seizure occurred at 13:41, 41 minutes into session 5, whilst doing word puzzles. This seizure was electroclinically similar to the 12 other seizures the patient experienced during their 5 day admission and was described by him as a habitual attack.

**LS3** A 23 year old male with a year history of seizures of unknown aetiology reported no family history of epilepsy. His seizure frequency was estimated to be several per day. During telemetry, his interictal EEG comprised of occasional bursts of sharp and slow wave complexes which increase in frequency overnight. The ictal features were:- (i) clinically suggestive of

absences (eg abrupt brief disruption in conversation albeit with no motor phenomena) (ii) electrographically showed enhanced bursts of paroxysmal slow or sharp wave activity. It was felt that these features were representative of primary generalised epilepsy. MRI found widening of the cerebral spinal fluid spaces with no focal pathology. His medication on admission was Sodium Valporate 1200mg, Phenytoin 375mg and Vigabatrin 2000mg. Drug reduction was not instituted. The leisure period absence seizure occurred whilst the subject was engaged in conversation (40 minutes into session 8). The absence was electrographically similar to one other seizure the subject experienced during admission. The subject indicated that the leisure seizure was the same as his habitual events.

**LS4** A 22 year old female with a 7 year history of seizures reported no family history of epilepsy or other potential aetiology. Her seizure frequency was estimated to be between 1-5 seizures per day. During telemetry, her interictal EEG showed (a) clear intermittent background abnormality over the right temporal region and (b) independent bitemporal spikes. The three clinical seizures:- (i) electrographically originated from the right temporal region and were (ii) clinically compatible with temporal lobe fits, although one other electrographic seizure was definitely left-sided. Two MRI scans were reported as normal. Her medication on admission was Carbamazepine 700mg, Lamotrogine 200mg and Topiramate 100mg. Drug reduction was not instituted. The leisure period seizure occurred at 16:29, 19 minutes into session 8, whilst the subject was writing a letter. The leisure-period seizure was electroclinically similar to two other spontaneous seizures experienced during a 3 day stay on the unit.

**LS5** A 35 year old male with a year history of seizures reported no family history of epilepsy or other potential aetiology. His seizure frequency was estimated to be 1-2 per day. During telemetry, his interictal EEG displayed moderate abnormalities in background activity with spikes that were predominantly right-sided and maximal in the right temporal region. The recorded seizures gave no clear electroclinical pattern of localisation or lateralisation but were likely to be extratemporal. MRI studies were reported to have shown both a right occipital lobe lesion and abnormal gyrii. His medication on admission was Phenytoin 300mg, Carbamazepine 1200mg and Lamotrogine 200mg. Drug reduction was not instituted. The leisure period seizure occurred at 14:49, 19 minutes into session 2, whilst the subject was watching television. The leisure-period seizure was electroclinically similar to the majority of the 23 spontaneous clinical seizures suffered during the five-day admission.

**LS6** A 47 year old man with a year history of seizures reported no family history of epilepsy or other potential aetiology. His seizure frequency was estimated to be 3-4 per day. During telemetry, his interictal EEG showed bitemporal background and epileptiform abnormalities, more markedly on the left. The clinical seizures were characterised by:- (i) left-sided lateralisation, best seen temporally, electrographically and (ii) features compatible but not typical of TLE clinically. MRI were reported as normal, although a slight right-sided atrophy was noted on volumetric analysis. His medication on admission was Phenytoin 200mg, Carbamazepine 1200mg and Clobazam PRN. Drug reduction was not instituted. The leisure period seizure occurred at 15:11, 6 minutes into session 3, whilst the subject was reading. The leisure-period seizure was electroclinically similar to 8 other spontaneous seizures suffered during the subjects five day admission to the unit.

**LS7** A 28 year old male reported no family history of epilepsy and no other potential seizure-disorder aetiology. His seizure frequency was estimated to be 3-4 per month. During telemetry, his interictal EEG MRI studies showed evidence of left hippocampal sclerosis. His medication on admission was Carbamazepine 1800mg and Clobazam 20mg. Drug reduction

was instituted. The leisure period seizure occurred whilst the participant was engaged in conversation at 17:09, 34 minutes into session 5.

**LS8** A 28 year old male with seizures of unknown aetiology. His seizure frequency was several per day. During telemetry, his interictal EEG was maximum at the right mid-frontal region. The clinical features of his seizures suggested an extratemporal focus, although this could not be confirmed with EEG records, which were unhelpful for localisation. MRI studies found no abnormalities. His medication on admission was Lamotrigine 600mg and Carbamazepine 1400mg. The leisure period seizure occurred at 16:24, 39 minutes into session 4, whilst the participant was engaged in reading. It was one of more than twenty clinical seizures witnessed during a 3 day admission, all of which were electroclinically similar.

**LS9** A 28 year old man with seizures of unknown aetiology reported a seizure frequency of 3-4 per month. During telemetry, his interictal EEG showed infrequent left temporal spikes. He had ictal recordings compatible with left TLE. An MRI study was reported to show left hippocampal sclerosis. His medication on admission was Carbamazepine 1800 mg and Clobazam 20mg. Drug reduction was instituted. The leisure period seizure occurred at 17:05, 30 minutes into session 5, whilst the participant was engaged in a brief conversation. It was the only seizure recorded during telemetry but was similar to those described by relatives in the medical notes.

**LS10** A 48 year old male developed habitual seizures one year after suffering a severe head injury aged 6. He estimated that he suffered up to 4 seizures a week. During telemetry, he demonstrated no interictal EEG abnormalities and his seizures were consistent with an extratemporal focus. MRI studies reported evidence of a longstanding generalised atrophy in the left cerebral hemisphere, most marked in the temporo-parietal region. His medication on admission was Carbamazepine 1600mg and Clobazam 40mg. Drug reduction was instituted. The leisure period seizure occurred at 14:19, 34 minutes into session 6, whilst the subject was listening to music. It was electroclinically similar to several other seizures experienced by the participant during his 5 day admission.

**LS11** A 28 year old male reported experiencing a febrile convulsion aged 18 months. His seizure frequency on admission was estimated to be 2-3 per week. His video and EEG-telemetry recordings were found to be compatible with left temporal lobe epilepsy. MRI studies reported left hippocampal sclerosis. His medication on admission was Carbamazepine 1400mg, Clobazam 20mg, Lamotrigine 100mg and Gabapentin 2100mg. Drug reduction was instituted. The leisure period seizure occurred at 18:00, 35 minutes into session 6, whilst the subject was watching television. It was electroclinically similar to five other seizures that the patient experienced during his admission and was described by him as habitual.

**LS12** A 28 year old female reported a 3 year history of seizures. She estimated that she suffered approximately 4-5 seizures per month, although they occasionally clustered. Her interictal EEG recording was unremarkable except during voluntary hyperventilation which produced some rare right temporal sharp waves. She experienced 18 habitual episodes during her 5 day recording, were all electroclinically similar. MRI studies revealed a suspected DNT in the right temporal lobe. Her medication on admission was Phenytoin 300mg which was reduced. The leisure period seizure occurred at 14:01, 31 minutes into session 1, whilst the participant was reading. It was similar to all of the other seizures she experienced during her admission and the patient described it as habitual.

**Table 6** Summary of seizure group characteristics (N=25)

Parameter	
Gender	8 females, 17 males
Age	Median 29 years, Interquartile range 26-37 (Range 18-57)
Possible Aetiology	Febrile convulsion (6), Head trauma (3), Encephalitis (1), Other (1), None known (14)
Imaging Abnormalities	Focal (19) [Temporal (16), Extratemporal (3)], Generalised / Multifocal (2), Normal (3), No imaging (1)
Seizure type	Absence (1), Simple partial (13), Complex partial (24), Generalised tonic-clonic (13) [ 1 type (4), 2 types (18), 3 types (3)]
Seizure Frequency	> 1 / day (11), 1-6 / week (9), 1-4 / month (5)
AED combination	Monotherapy (2), Two AED's (13), Three or more AED's (10)

The demographic and clinical features of those patients who experienced seizures during the study was similar to the whole sample with the exceptions of seizure frequency and gender. Subjects with a history of frequent seizures were, as expected, well represented in seizure group. More male subjects suffered seizures during the study programme, although the gender difference was not statistically significant (chi-squared = 2.62).

### 7.3 Detailed description of results

**Table 7** Results Summary One - Outcome by patient

Overall proportion with seizures	25 / 212 (11.8%)
(95% CL)	(7.5, 16.1)
Proportion with VG Seizures	13 / 212 (6.1%)
Proportion with L Seizures	12 / 212 (5.7%)
Difference between % (VG - L)	0.47% (-4.1, 5.1%)

**Table 8 Results Summary Two - Outcome by session**

	VG	L	Total
Number of patients having seizures	13	12	25
Number of sessions	809.5	811	1620.5
Number of hours	607	608	1215
Hazard rate (per hour)	0.021	0.020	0.021



**Table 9** Special features of seizure group

<i>Whole Sample</i>	<b>Seizure group</b>			
		Total seizures	VG seizures	L seizures
Sleep deprivation	24%	4/25 (16%)	3/13	1/12
AED reduction	59%	16/25 (64%)	9/13	7/12
Pre-seizure tachycardia and / or hyperventilation		0/25 (0%)	0/13	0/12

Partial sleep deprivation did not feature more prominently in the video-game seizure group in comparison with the whole study sample. This is despite the fact that all sleep deprived studies took place at a later stage of the patient's admission (Wednesday or Thursday); ensuring that average serum drug levels of the sleep deprived group were lower than that of the whole sample.

Examination of the ECG record and video display did not show any evidence of hyperventilation and / or tachycardia, which may be regarded as indicators for changes in arousal / excitement, in the 5 minutes preceding the seizure onset in any instance.

**Table 10** Timing of seizure occurrence

**V** = Video game playing seizure  
**L** = Other leisure activity seizure

Time of Seizures	Minutes				
	0-9	10-18	19-27	28-36	37-45
Session No.					
One	V / L				
Two			L		
Three	V / L				
Four		V		V	L / V
Five				L	L
Six		L / V / V		V / L / L	
Seven				L / V	V
Eight		V	V / V / L	L	

Length of play within one session was not found to have any affect on the likelihood of seizure occurrence as the study program seizures were equally distributed throughout the 45 minute sessions.

**Table 11** Timing of seizure occurrence\* (Crude analysis)

<u>Time after the start of session 1</u>	<u>Number of seizures</u>
000 - 105 minutes	3
105 - 210 minutes	6
210 - 315 minutes	11
315 - 420 minutes	13
[ 2 hours post-study ]	10

\*includes all meal-break seizures (n=8)

Sessions of 45 minutes duration interrupted by a meal-break of 45 minutes  
after session 6 on Tuesdays and of 60 minutes after session 4 on Wednesdays  
and Thursdays

Weibull Model

Number of cases read 250

Cases with use set to zero 11

Remaining number of cases 239

Status Code Frequencies

<u>Total</u>	<u>Seizure*</u>	<u>OK</u>	<u>Proportion Censored</u>
239	43	196	0.82

\*includes all study period seizures (25), all meal-break seizures (8) and seizures in the 2 hours after the study (10)

**Table 12** Accelerated Failure Time Model

<u>Variable</u>	<u>Co-efficient</u>	<u>Standard Error</u>	<u>Coeff / SE</u>	<u>Exp</u>
(Coeff)				
-1 Constant	7.34	0.19	37.8	1538.94
-2 Scale	0.69	0.10		1.98

To test for difference from 1 we get:-

$$\text{(Normal Deviate), } z = \frac{1-0.69}{0.10} = \frac{0.31}{0.10} = 3.1$$

which is associated with  $p < 0.005$

So the scale parameter (AFT model) is significantly less than one

⇒ shape parameter (Weibull model) is significantly  $> 1$

⇒ hazard increases with time (or session)

## **8 Study Four**

### **A study of the relationship between participation in common leisure activities and seizure occurrence**

This study sought to investigate whether participation in the main programme of fairly intensive leisure activities (video games, reading, doing word puzzles, watching television, doing physical exercise) lead to an overall increase in seizure occurrence in the study group. A retrospective analysis of the video-EEG reports of all participants was undertaken to determine the number of clinical seizures which occurred on the day(s) that they did not participate in the activities programme (Rest Days). Depending on the length of the admission of each participant, the number of whole days available for analysis varied between zero and two. For a meaningful comparison, only first seizures occurring within the same time slots allocated to the activities programme (excluding those during the meal-break) were counted during the rest days. Participants were not given instructions of the types of activities to pursue on the rest days. Informal observation of participants throughout the study indicated that they were engaged in far less demanding tasks on the rest days compared with those undertaken during the structured activities program.

#### **Analysis**

The occurrence of seizures was noted for both the activities day and the rest days for each subject. The relative risk of seizure occurrence (together with its 95% confidence interval) on an activities day compared with a rest day was calculated using the methods for a matched case-control study with varying number of controls (Breslow and Day 1980).

## Results

Of the 212 participants who either completed the activities programme or experienced a seizure during one of the eight leisure sessions, 155 could be compared on two and 29 could be compared on one whole Rest Day(s). No comparison days could be analysed with 22 participants as their admission was too brief and the video-EEG reports of the remaining 6 participants were unavailable.

**Table 13 Seizure occurrence on activities and rest days in 184 participants**

	Subjects having only one rest day (n=29)		Subjects having two rest days (n=155)		
	No seizure on only rest day (n=26)	Had seizure on only rest day (n=3)	No seizure on either of two rest days (n=120)	Had seizure on one of the two rest days (n=31)	Had a seizure on both of the two rest days (n=4)
Had seizure on activity day (n=17)	1	1	11	3	1
Did not have seizure on activity day (n=167)	25	2	109	28	3

Maximum Likelihood Relative Risk (95% CL): 0.71 (0.38, 1.33)  
 $(\chi^2 = 0.8, df = 1, P > 0.3)$

*(Relative Risk = 0.71)*

<sup>seizure</sup>  
 The risk of seizures was lower during activities days (~~0.71~~) but not significantly so with a wide confidence interval.

Our results demonstrate that participation in a structured programme of fairly intensive activities, requiring both mental and physical effort, did not appear to increase the likelihood of seizures compared with periods of relative rest in a large, representative sample of chronic epilepsy sufferers.

## 9 Discussion

The major finding of this research is that video game play did not present a substantially greater risk for seizure occurrence compared with participation in other common leisure pursuits within a large sample of chronic epilepsy sufferers without known visual sensitivity (although due to the small numbers involved, a greater risk of seizures during video game play in the general epilepsy population cannot be ruled out entirely). 25/212 subjects experienced a clinical seizure during the study program; thirteen seizures occurred during periods of video-game play and twelve during periods of alternative leisure. No new form of reflex epilepsy associated with video-game play was identified in the population studied. A subsidiary finding was that no significant alteration to seizure susceptibility was witnessed during participation in the overall program of structured leisure activities, compared with periods of relative rest.

The proportion of patients admitted to the unit who were identified as visually-sensitive (4.3%) was within the anticipated range for the study population and accord with prevalence rates reported elsewhere (Harding and Jeavons 1994, Kasteleijn-Nolst Trenite 1989). Most (9/11) of the identified cases of photosensitivity were not newly diagnosed but had demonstrated Type 4 photosensitive response (Waltz et al 1993) on a previous EEG investigation.

The study design was a modification of a conventional parallel-group trial, which would have required patients to be randomised solely to video-games or leisure activities. Such a design was not practical here because participants could not spend up to 6 hours engaged in almost continuous video-game play.



Instead alternation of the two types of activity was arranged with participants randomised to video-games or leisure in the first session.

The present study has taken somewhat of an atypical approach to the investigation of reflex epilepsy or 'precipitated' seizures and therefore a direct comparison of the findings with other studies is not possible. It is unique as it sought to **prospectively** investigate the effects of video-game play on seizure occurrence in a large representative population of chronic epilepsy sufferers. This approach has allowed systematic experimental manipulation of certain, possibly provocative, aspects of video-game play ie sleep deprivation and length of play whilst attempting to provide a naturalistic setting. Conducting the studies on a video EEG-telemetry facility has allowed a comprehensive documentation of the visual, EEG and physiological parameters associated with a number of video-game seizures and granted immediate access to the individuals concerned. All previous studies of 'video-game epilepsy' have been forced to rely on retrospective account of events from patients and relatives. Unfortunately, in many cases this has only allowed speculation of the likely association between stimulus and seizure, rather than causal one, as this approach involves uncontrolled observations of distant events. Furthermore, the majority of published cases involve a single instance of a video-game seizure and are therefore incompatible with both the formal classification systems (Commission on Classification and Terminology of the International League Against Epilepsy 1989) and classical (Hume 1739) requirements for establishing causality.

Previous investigations may have overrepresented some of the more unusual varieties of video-game seizures. The general reflex epilepsy literature is littered with examples of rare but fascinating conditions overshadowing its more common but mundane forms. The overwhelming majority of submissions at the most recent colloquium on reflex seizures and epilepsies at Geneva in 1988 dealt with rare but interesting forms whereas only 8 dealt with PS and none with startle epilepsy, which are by far the two most common forms of RE (Gastaut et al 1989). Investigators of VGS (or physicians referring them) may fail to highlight some of the more 'straightforward' cases, with demonstrable VS, and unwittingly select more interesting cases with uncertain aetiology to study.

Visual sensitivity, which is thought to be the major risk factor for VGS, has only been demonstrated in approximately one half of the documented cases. The two other sub-groups which feature prominently in a number of studies include patients in whom:- (i) non-photic aspects of video-game material were thought relevant (ii) the posterior regions / occipital lobe of the brain was implicated.

### 9.1 Potential non-photic precipitants of video-game seizures

Some investigators have suggested that certain non-photic aspects of this material may not only contribute to the genesis of VGS in cases who demonstrate VS but that they could also act as independent risk factors in those who do not. In a series of 15 patients Ferrie et al (1994) felt that emotional excitement, sleep deprivation, prolonged play and cognitive mechanisms were relevant in the genesis of certain VGS individuals not

demonstrating photosensitivity. A further report from Seattle (Graf et al 1994) in which 6/10 VGS cases were not photosensitive postulated that fatigue and sleep deprivation may be significant contributing factors. Results from a series of 23 VGS patients from Japan (Kato et al 1994), only 10 of which were photosensitive, led the authors to suggest that 'other factors are involved in the inducing mechanism of video games seizures as well (as PS)'. The Video-game Epilepsy Consensus Group (Binnie et al 1994) stated that non-photic factors such as decision-making, non-specific emotional factors or sleep deprivation could 'act either singly or in combination (with photic factors)' to promote seizure occurrence during video-game play. The present study has found no evidence in support of a significant role for non-photic aspects in the genesis of video-game seizures within our large sample despite exhaustive systematic inquiry.

#### 9.1.1 Excitement

Video game play has been associated with mild increases in certain physiological parameters, which are likely to reflect emotional excitement. Gwinup et al (1983) reported minor increases in blood pressure and heart rate in 23 young men during video-game play compared to periods of rest. Segal et al (1991) assessed the metabolic and cardiovascular responses to video-game play in 32 males and females aged 16-25 years. Heart rate, blood pressure and oxygen consumption were measured serially over thirty minutes while subjects played 'Ms PacMan'. Compared to periods of rest all three variables showed significant increases during video-game play. However, the level of exertion was thought to be comparable only to that of mild-intensity exercise such as walking at 2 miles an hour. Mazin and Etter (1984) studied six subjects (aged

10-41) for changes in blood pressure during video game play. Six different games were played for five minutes each with half an hour break in between each play. The average blood pressure (mm Hg) of the six subjects were as follows:- Pac-Man 114/70, Carnival 133/67, Space Invaders 117/73, Bowling 108/62, Kaboom 118/74 and Night Driver 117/66 compared with the average baseline rate of 106/62 mm Hg. The authors concluded that video game play lead to an increase in blood pressure, with the most exciting games facilitating the greatest increases. Hyperventilation, which may also be considered to be indicator of excitement, has been cited as a potential risk factor for video-game seizures (Dalquist et al 1983). However, the relevance of emotional excitement / physical exertion in the genesis of VGS is uncertain as these factors have not been reliably linked to an alteration of seizure susceptibility in the general epilepsy literature (refer Introduction). The present study did not find a role for excitement in the genesis of any study period seizures (VG or L). Although blood pressure was not measured, examination of the ECG record and video display did not show any evidence of hyperventilation and / or tachycardia in the 5 minutes preceding the seizure onset in any instance.

#### 9.1.2 Sleep deprivation (SD)

SD has been linked to an of enhancement of the photoparoxysmal response (PPR) in certain PSE sufferers (Scollo-Lavizzari and Scollo-Lavizzari 1974) and has also been implicated in a number of the documented cases of VGS. Cook and Hoskins (1992) reported that one of their two VGS cases was 'very tired having had only 2 hours sleep the previous night'. Helfgott and Meister (1983) reported that an 8 year old boy suffered a seizure whilst playing an

arcade game after obtaining little sleep the night before due to car travel and was also fatigued from several hours of skiing. Graf et al (1994) stated that sleep deprivation and / or fatigue were common among a sample of 10 video game-related seizures, although specific details were not reported. Ferrie et al (1994) reported that 1/15 of their sample was sleep deprived on the night before the seizure. In a major epidemiological survey of incident cases of seizures associated with video-game play, Quirk et al (1995) found that sleep deprivation was implicated in 11/118 cases (9%).

The role of sleep deprivation in VGS cases not demonstrating VS is unknown. There is no current evidence to suggest that sleep deprivation reduces the seizure threshold to photic material in individuals who do not harbour the photosensitive trait. Some investigators have suggested that SD could combine with certain non-photoc aspects of video-game material to enhance risk (Ferrie et al 1994, Binnie et al 1994). However, it is also possible that SD will increase the susceptibility to a fortuitous seizure during subsequent exposure to video-game material (Kasteleijn-Nolst Trenite 1994). The present study did not find sleep deprivation to be overrepresented in our video-game seizure group. Partial sleep deprivation was undertaken by 24% of the whole sample prior to the study, yet only 16% of the total seizure group and 23% of the video-game seizure group were sleep deprived. This is despite the fact that all sleep deprived studies took place at a later stage of the patient's admission (Wednesday or Thursday); ensuring that average serum drug levels of the sleep deprived group were lower than that of the whole sample.

### 9.1.3 Length of play

In a published set of guidelines aimed at reducing the risk of seizures, Binnie et al (1994) state that video-game play should be restricted to less than 1 hour in any one session. Selected articles in the media, both print and electronic, as well as game packaging have also cautioned all players to take regular breaks from play (Daily Mail 7/1/93). However, the foundations of these warnings is uncertain as prolonged play has seemingly been implicated in only two of the > 200 documented cases (Hart 1990, Ferrie et al 1994). In their study of 118 presenting cases, Quirk et al (1995) found no evidence to suggest that prolonged play in a single session was more hazardous. The results from this study cannot rule out the possibility that prolonged exposure time does increase the risk of a video-game seizure as subjects only played for a maximum of forty-five minutes in any one period. However, there was no evidence to suggest that the length of exposure within this forty-five minute period was a risk factor as an approximately equal number of seizures was recorded at the beginning, middle and end of the sessions.

### 9.1.4 Fatigue / Arousal

Fatigue will naturally result after sleep deprivation and / or prolonged play over a number of sessions in the same day. Results from the present study suggest that fatigue may have an effect on seizure occurrence generally as there was clear evidence that a greater number of seizures occurred in the latter sessions. This pattern could also be explained in terms of a gradual loss of the protective effects of arousal throughout the study (Vidart and Geier 1968, Guey et al 1969). However, there did not appear to be any evidence to

suggest that fatigue and / or arousal loss combined with certain aspects of video-game play to promote any excess seizure risk as an approximately equal number of video-game and alternative leisure seizures were witnessed in the later sessions. This suggests that fatigue / arousal loss factors were operating per se. This increased seizure rate in the later sessions was unlikely to be a reflection of decreased AED serum levels as the total study duration was only a 7 hours; a period that would not normally be associated with a substantial decrease in serum levels.

Certain aspects of video-game play, such as the level of cognitive engagement, are for obvious reasons difficult to manipulate and measure. However, the overall seizure tally (13 vs 12) suggests that it, or any combination of the above factors, had a negligible bearing on seizure occurrence.

## 9.2 Partial video-game seizures in individuals negative to IPS

The occipital lobe has been implicated in a small proportion of published video-game seizure cases. Ferrie et al (1994) found evidence of a posterior epileptic focus in one-third of their series of 15 patients; 4/5 of which were negative to IPS. However, other reports implicating a posterior focus in the absence of VS appear to be isolated (De Marco and Ghersini (1985) - 1 case, Graf et al (1994) - 1 case, Fish et al (1994) - 1 case). These patients may harbour a special type of photosensitivity (Binnie 1998) which require unusual methods of visual sensitivity testing, eg for fixation-off sensitivity, to elicit a positive response (Ferrie et al 1994). Ricci and Vigevano (1993) suggest that occipital seizures provoked by light stimulation probably

represent an exaggeration of the 'posterior response' observed in photosensitive patients. However, such cases are likely to be very rare as occipital seizures are thought to affect only 2-3% of the general epilepsy population and there is no evidence to suggest that reflex seizures are commoner in this group (Sveinbjornsdottir and Duncan 1993).

The present study investigated 8 patients with an occipital focus, in keeping with its rarity. Interestingly, 1/8 experienced a VGS during the study. However, on questioning this patient stated that she had not experienced any seizures associated with video-game material in the past, despite substantial previous exposure.

### 9.3 Chance association between video-game play and seizures

The possibility of a coincidental association between video-game and seizure in individuals without visual sensitivity was emphasised in The National Survey of Photosensitivity and Seizures Induced by Electronic Screen Games (Fish et al 1994) which investigated virtually all presenting seizures associated with video-game play throughout Great Britain over two three month periods in 1993 and 1994. 118 cases were identified. The sample were split into three groups:- [A] those for whom there was thought to be a definite causal relationship between video-game and seizure (46) [B] those for whom the causal relation was probable (25) and [C] those for whom it was thought that no causal relation was apparent (47). The criteria used for excluding a causal relation was an absence of a photoparoxysmal response during IPS or any other evidence suggesting photosensitivity such as a further seizure on re-exposure to a video-game or any other photic source. In order to justify the



classification of Group C cases as coincidental to video-game exposure, the authors calculated a crude estimate of the number of 'chance' video-game seizures (causally unrelated, temporally coincident) that were likely to be identified during the study period. This estimate was derived using approximate figures for:- (i) the average daily exposure to video game material in 7-19 year olds (BRMB International 1993) (ii) the incidence of epilepsy not demonstrating photosensitivity in this age group and (iii) the population of Great Britain (GB) in this age group. The actual number of Group C cases did not exceed the expected figure (38 v 66). The lesser number of actual cases was taken as evidence to support the hypothesis that the presence of the photosensitive trait represents the main if not sole risk factor for video-game seizures in incident cases. Results from the current study provide strong support for this hypothesis within the known epilepsy population, ie seizures during video-game play in the > 95% of the epilepsy population without visual sensitivity are most likely to represent a chance occurrence.

Despite some early caution, other research groups have recently suggested that visual sensitivity may be the sole or main risk factor for video-game seizures. Referring in part to her own unpublished work of 87 photosensitive or video-game sensitive patients Kasteleijn-Nolst Trenite (1994) asserts that 'patients without any evidence of photosensitivity - ie 95% of all epileptic patients - have no excess risk of experiencing a seizure while playing a video game'. Reviewing nine of their own cases and the literature Harding et al (1994) argued that the video-game seizure population is not distinguished from the photosensitive population by age, gender or in other important characteristics.

It is likely that patient groups with substantial exposure levels to video-game material could be expected to suffer one or a number of coincidental seizures during play. In their studies of 'television epilepsy' Gastaut et al (1962) noted that patients whose average daily exposure to television is four hours can expect approximately one quarter of their daytime seizures to be associated with this material. However, the scope for a chance association between video game and seizure emphasised in the current study should always be considered a likely rather than definite explanation in individual video-game seizure cases not demonstrating visual sensitivity. There can be no absolute certainty that all of the individual video-game seizures suffered during the present study were a coincidence, despite a high probability of them being such.

#### 9.4 Potential methodological shortcomings of the present study

The present study has some potential shortcomings. One concern is whether the study sample was representative of the wider epilepsy population. A high proportion of participants in our sample had a seizure typology and/or MRI/EEG features suggestive of partial epilepsy. It would have been desirable to study a more heterogeneous sample although it has been shown that sufferers of partial onset seizures can account for up to two-thirds of all cases of epilepsy (Hauser and Kurland 1975, Zielinski et al 1974). Our sample more accurately reflects a chronic population in which sufferers of partial seizures feature prominently as they are more commonly medically intractable than other seizure types (Mattson et al 1985). Nonetheless, the fact that no differences were found in seizure susceptibility during video-game play or other leisure sessions in the 18 (8.5%) subjects who had primary

generalised or multifocal epilepsy provides some support for generalising our findings to the wider epilepsy population.

Our sample had no children or adolescents as the study took place in an adult hospital. Whilst it would have been desirable to also study this group, as they represent the main users of video-game material, it is likely that many would not have been compliant with the study program. Both the length of commitment (7 hours) and the necessity for strict adherence to the fixed session times might have resulted in an unacceptable number of participant withdrawals.

The present sample were likely to have an extremely low seizure threshold during their study participation. Virtually all had chronic epilepsy and suffered fairly frequent seizures, 59% were substantially drug-reduced and 24% were partially sleep deprived during their participation in the study. It is arguable that any increased susceptibility to seizures during video-game play in the general epilepsy population, including children and adolescents, would have been demonstrated in our very low seizure-threshold sample.

It is essential to recognise, as was highlighted in the Introduction, that occasional subjects with reflex epilepsy / seizures not associated with visual material may have their seizures precipitated by certain aspects of video-game play ie thinking, movement, startle. Maeda et al (1990) has described two patients in which sensitivity was demonstrated to video-game play but not during VS testing. However, reflex epilepsy / seizures without VS appear to be very rare and may only account for < 1% of the total epilepsy population

(Roger et al 1989). Furthermore, it is unlikely that seizure precipitation via these mechanisms will exclusively manifest as video-game seizures as other everyday activities may also utilise these functions

#### 9.5 The effect of study participation on seizure occurrence

A subsidiary aim of the present investigation was to determine whether participation in the activities study (video game and leisure sessions) had any overall bearing on seizure occurrence by comparing it to Rest Days. The risk of seizures was not found to be significantly higher on the activities day compared with other days of relative rest ( $p>0.3$ ). This finding contrasts the view held by many patients with epilepsy who anecdotally report that attention to a task increases the likelihood of seizure occurrence. Antebi and Bird (1993) state that 29% of 100 patients attending a tertiary referral centre reported that concentration to a task increased the frequency of their seizures. In a survey of seizure precipitants reported by mothers of 237 children with frequent seizures (Verduyn et al 1988), being 'alert and concentrating' had some association with seizures in 60% of the sample, although a 'relaxed state' was thought to be implicated in the genesis of seizures for 75% of the same sample. In contrast to these studies, Servit et al (1962) found that 'concentration of attention on a certain activity' was reported to inhibit seizures by 18% of 895 patients attending two Medical Advice Centres for Paroxysmal Disease in Prague. 13% of this sample reported that 'idleness or physical and mental relaxation' increased the occurrence of their seizures. Studies which rely on self-report are difficult to interpret. Research has shown that illness cognitions held by chronically sick people can commonly focus on the 'causes' of their disease (Leventhal et al 1980). Many individuals

who suffer from epilepsy appear to be eager to seek an explanation of why their seizures occur, which can lead some patients to wrongly attribute certain coincidental stimulus / states as precipitating factors. Antebi and Bird (1992) have suggested that this can help create cognitive distortions such as 'I am unhappy today and I have had an attack, therefore any time I have an attack it must be because I am unhappy'.

#### 9.6 Patient perceptions of risk associated with video-game play

My initial questionnaire study found that 10% of 364 patients attending a specialist neurology treatment centre in London indicated that they felt that their seizures could be triggered by video-game play. Furthermore, 41% of those surveyed indicated that they believed that flashing lights precipitated their seizures.

It is difficult to ascertain precisely why such a marked difference between perceived and real risk has come about. With regards video-game material, the press barrage of 1993 may have contributed to some of the potential misinformation. Suggestions that (i) 'individuals with (non-photosensitive) epilepsy stay up all night playing these games which seems to make them light sensitive' (Daily Telegraph 22/9/93) and (ii) 'video games lead to medical problems such as epilepsy' (The Guardian 14/2/93) are unsubstantiated. More recently, in response to convulsions suffered by approximately 700 Japanese children whilst viewing 'Pocket Monsters' it was reported that:- (i) 'it is quite common for people who are prone to epileptic fits to have an attack brought on by looking at flickering TV screens or computer monitors' (The Sun 18/12/97) and (ii) 'a flickering television or computer screen can trigger a

convulsion in anyone, especially if they have been sitting in front of it for a long time' (The Independent 18/12/97). Both statements arguably overestimate the number of people who at risk from this material. Video-game packaging also carries warnings about potential risks, for example the SuperNintendo range warns: 'Consult your physician before playing video games if you, or anyone in your family, has an epileptic condition'. Such warnings appear to implicate a great number of people. The results from my second questionnaire study strongly suggest that inadequate education and misinformation may also have contributed to peoples' concerns regarding video-game play.

#### 9.7 Redefining RE?

Some investigators have suggested that the term 'reflex epilepsy' should be abandoned or its definition relaxed to include individuals with a less unequivocal association between stimulus and seizure, incorporating patient perceptions (Antebi and Bird 1992). The results of the present study have helped to demonstrate the existence of a marked difference between patient perceptions of risk associated with a video-game material and the real and known risks of play. Similar over-estimates of risk may be commonplace as there is good evidence to suggest that a substantial proportion of epilepsy patients have concerns regarding seizure occurrence during exposure to other visual material (Millett et al 1997) as well as during engagement in particular life situations (Fenwick and Brown 1989). A relaxation or abandonment of the current definition(s) of reflex epilepsy / seizures requires careful consideration as this may further encourage patients to avoid particular stimuli / states inappropriately.

The present study did not identify a new form of reflex epilepsy associated with video-game play. It appears that visual sensitivity is the main indicator of susceptibility to causally-linked video-game seizures. All patients with epilepsy do require comprehensive testing for visual sensitivity, particularly those who suffer their first seizure in childhood and adolescence. In general, those without visual sensitivity should be informed that they are at an extremely low risk of experiencing a causally-related seizure associated with video-games or other photic material and if an isolated attack occurs in such a setting then it is probably due to chance. The provision of accurate advice to all epilepsy patients is important as individuals who are under-educated or misinformed regarding the risks posed by video-games or other visual material may restrict their lifestyles inappropriately (Millett et al 1998; questionnaire study two). However, it is essential that all seizures associated with video-game material be assessed on an individual patient basis.

Giving advice on an individual patient basis can be difficult as some may have views regarding the timing of their seizures which are resistant to change. It is important to respect each patient's perspective, as they are in the best position for judgement. However, it may be worthwhile to emphasise to concerned individuals that people with epilepsy must be doing something when seizures occur, ie work, exercise, rest, and that the degree of association between a specific type of activity and seizure occurrence is most likely to be a function of the time spent pursuing it.

### 9.8 Directions for future research

The present study has taken a somewhat atypical approach to the investigation of reflex epilepsy or 'precipitated' seizures. Prolonged access to a suitable and willing population in a specialist setting ~~were~~<sup>was</sup> necessary in order to carry out this project. These favourable conditions may be difficult to replicate elsewhere. The project was very labour-intensive as all (247) subjects had to be closely monitored throughout their participation in the activities programme. Despite these difficulties, prospective studies should be considered (where possible) as they represent the best means of determining the nature of the association (causally related or temporally coincident) between stimulus and seizure in groups of patients thought to suffer from the non-visual reflex epilepsies.

Future research into video-game seizures should involve further scrutiny of cases not demonstrating visual sensitivity. Where there is evidence of a causal relationship in individual cases, eg documented pattern of seizures on re-exposure, a detailed exploration of specific risk factors is warranted.

Confirmation of the findings of the present study in other populations, most notably in children and adolescents, would be desirable.



## **References**

Aguglia U, Tinuper P, Gastaut H (1984) Startle-induced epileptic seizures.

*Epilepsia* 25(6):712-20.

Alajouanine Th and Gastaut H (1955) La syncinesie-sursaut et l'epilpsie-sursaut a declenchement sensoriel ou sensitif inopine. Les faits anatomocliniques (15 observations). *Rev Neurol* 93:29-41.

Allen A and Morrow J (1994) 'Sonic, Tonic, Clonic': three cases of video game epilepsy. *Ulster Medical Journal* 63(1):99-102.

Ambrosetto G and Tassinari CA (1987) Photosensitivity related to valporate withdrawal. *Journal of Neurology, Neurosurgery and Psychiatry*, 50, 1709-10 (Letter)

Anderson N and Wallis W (1986) Activation of epileptiform activity by mental arithmetic. *Archives of Neurology* 43:624-6.

Antebi D and Bird J (1992) The facilitation and evocation of seizures. *British Journal of Psychiatry* 160:154-64.

Antebi D and Bird J (1993) The facilitation and evocation of seizures. A questionnaire study of awareness and control. *British Journal of Psychiatry* 162:759-64.

Barker W, Burgin S, Simons D (1950) The significance of 'spontaneous' abnormalities in brain wave patterns as observed during interview with epileptic patients. *JNMD* 112(3):187-205.

Beagonhole R, Boniton R, Kjellstrom T (1993) Basic epidemiology. *WHO Geneva*.

Beaumanoir A, Volanschi M, Volanschi D, Roger G (1989) Reflex (sensory evoked) seizures in a population of epileptics aged less than 15. In Beaumanoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies*. Geneva: Editions Medicine et Hygiene pp 475-478

Bennett D (1963) Sleep deprivation and major motor convulsions. *Neurology (Minneap.)* 13:953-8

Binnie CD (1998) Simple reflex epilepsies. In *Epilepsy: A comprehensive textbook*. Eds Engel J Jnr and Pedley T. *Lippincott-Raven Publishers, Philadelphia* pp 2489-2505.

Binnie CD, Kasteleijn-Nolst Trenite D, Smit A, Wilkins A (1987) Interactions of epileptiform EEG discharges and cognition. *Epilepsy Research* 1:239-45.

Binnie CD (1993) Electroencephalography. In Laidlaw J, Richens A, Chadwick D (Eds) A textbook of epilepsy (4th Edn) *Churchill Livingstone, Edinburgh pp 277-348.*

Binnie CD, Harding GFA, Wilkins AJ, Richens A (1994) Video games and epileptic seizures - a consensus statement. *Seizure 3:245-246.*

Brenner R and Seelinger D (1979) Drawing-induced seizures. *Archives of Neurology 36(8):515-6.*

Brens S and Murray T (1984) Musciogenic epilepsy. *Canadian Medical Assoc. Journal 131(10):1255-58.*

Breslow NE and Day NE. Statistical Methods in Cancer Research. Volume 1: The Analysis of Case-Control Studies. *International Agency for Research on Cancer. Lyon, 1980.*

Brincotti M, Matricardi M, Pelliccis A, Trasatti G (1994) Pattern sensitivity and photosensitivity in epileptic children with visually induced seizures. *Epilepsia 35(4):842-849.*

BRMB International (1993) Youth TGI survey

Brock A (1929) Greek Medicine. *Dutton, New York pp 222*

Ch'en H, Ch'in C, Ch'u P (1965) Chess epilepsy and card epilepsy: two new patterns of reflex epilepsy. *Chinese Medical Journal* 84(7):470-4.

Cirignota F, Cicogna P, Lugaresi E (1980) Epileptic seizures during card games and draughts. *Epilepsia* 21:137-40.

Commission on Classification and Terminology of the International League Against Epilepsy (1989) Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 30(4):389-99.

Cook T and Hoskins M (1992) Video game seizures: technical considerations. *J Electrophysiol. Technol.* 18:175-84.

Covanis A, Gupta A, Jeavons P (1982) Sodium valporate: monotherapy and polytherapy. *Epilepsia* 23:693-720.

Critchley M (1937) Musicogenic epilepsy. *Brain* 60:13-27

Currie S, Heathfield K, Henson R, Scott D (1971) Clinical course and prognosis of temporal lobe epilepsy: a survey of 666 patients. *Brain* 94:173-190.

Daily Mail, United Kingdom 22/9/93

Daily Telegraph, United Kingdom 22/9/93

Dalquist N, Mellinger J, Klass D (1983) Hazard of video games in patients with light sensitive epilepsy. *JAMA* 249:776-777.

Daneshmend T and Campbell M (1982) Dark Warrior Epilepsy. *British Medical Journal* 284:1751-52.

Degen R, Rodin EA (1991) Epilepsy, sleep and sleep deprivation. *Amsterdam: Elsevier*

De Graaf A, Van Wyk Kotze T, Claassen D (1980) Photoparoxysmal responses in the electroencephalograms of some ethnic groups of the Cape Peninsula. *Electroencephalography and clinical Neurophysiology*, 50, 275-81

De Marco P and Ghersini L (1985) Videogames and epilepsy. *Developmental Medicine and Child Neurology* 27:514-21.

Descartes R (1664) *Traite de l'homme*. Angot, Paris. French text with English translation in Thomas Steele Hall (1972) *Treatise on man*. *Harvard University Press, Cambridge (Mass)*

Duncan J, Shorvon S, Fish D (1995) *Clinical epilepsy*. *Churchill Livingstone, New York pp 66-69*

Eriksen H, Ellerston B, Gronningsaeter H, Nakken K, Loyning Y, Ursin H (1994) Physical exercise in women with intractable epilepsy. *Epilepsia* 35(6):1256-64.

Esquivel E, Chaussain M, Plouin P, Ponsot G, Arthuis M (1991) Physical exercise and voluntary hyperventilation in childhood absence epilepsy. *Electroencephalography and clinical neurophysiology* 79:127-132.

Fearing F (1930) Reflex action. A study in the history of physiological psychology. *Williams and Wilkins, Baltimore*

Feldman R and Paul N (1976) Identifying emotional triggers in epilepsy. *Journal of Nervous and Mental Disease* 162(5):345-53

Fenwick P and Brown S (1989) Evoked and psychogenic epileptic seizures. I Precipitation. *Acta Neurol Scan* 80:535-40.

Ferrie CD, De Marco P, Grunewald RA, Giannakodimos S, Panayiotopoulos CP. (1994) Video game induced seizures. *JNNP* 57:925-931.

Ferrie C, Robinson R, Giannakodimos S, Panayiotopoulos C (1994) Video-game epilepsy. *Lancet* 344(8938);1710-11(Letter)

Ferry PC, Banner W, Wolf RA (1986) Seizure Disorders in Children. *Philadelphia: JB Lippincott*

Fish DR, Quirk JA, Smith SJM, Sander JWAS, Allen PJ (1994) National survey of photosensitivity and seizures induced by electronic screen games (video games, console games, computer games). *London: Department of Trade and Industry*

Forster F, Richards J, Panitch H, Huisman R, Paulsen R (1975) Reflex epilepsy evoked by decision making. *Archives of Neurology* 32:54-56.

Gastaut H (1989) Synopsis and conclusions of the International Colloquium on reflex seizures and epilepsies, Geneva 1988. In Beaumanoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies. Geneva: Editions Medicine et Hygiene pp 497-507.*

Gastaut H, Regis H, Bostem F (1962) Attacks provoked by television and their mechanisms. *Epilepsia* 3:438-45

Gataut H, Tassinari CA (1966) Triggering mechanisms in epilepsy. The electroclinical point of view. *Epilepsia*, 7, 85-138.

Gastaut H, Trevisan C, Naquet R (1958) Diagnostic value of electroencephographic abnormalities provoked by intermittent photic stimulation. *Electroencephalography and clinical Neurophysiology*, 10, 194-5 (Abstract)

Gibbs F, Gibbs E, Lennox W (1939) The influence of blood sugar level on the wave and spike formulation in petit mal epilepsy. *Arc Neurol Psychiat.* 41:1111-16.

Giroud M, Dumas R, Couillault G, Nivelon JL (1987) Les crises convulsives induites par les jeux video. *Archives of Francaises de Pediatrie*, 44, 397 (Letter)

Glista G, Frank H, Tracy F (1983) Video games and seizures. *Archives of Neurology* 40:588

Goossens L, Andermann F, Andermann E, Remillard G (1990) Reflex Seizures induced by card or board games, and spatial tasks: a review of 265 patients and delineation of the epileptic syndrome. *Neurlogy*, 40, 1171-6

Gowers WR (1881) Epilepsy and other chronic convulsive disorders. *Churchill, London.*

Graf WD, Chatrian G-E, Glass ST, Knauss TA. (1994) Video game-related seizures: A report on 10 patients and a review of the literature. *Pediatrics* 93(4):551-556.



Gross A and Clark V (1975) *Survival distributions: applications in the biomedical sciences*. New York, Wiley

The Guardian, United Kingdom 14/2/93

Guey J, Bureau M, Dravet C, Roger J (1969) A study of the rhythm of petit mal absences in children in relation to prevailing situations. *Epilepsia* 10:441-51.

Gwinup G, Haw T, Elias A (1983) Cardiovascular changes in video-game players. Cause for concern? *Postgrad-Med* 74(6):245-48.

Hall M (1833) On the reflex action of the medullar oblongator and medullal spinalis. *Phil Trans* 123:635-65.

Harding GFA and Jeavons PM (1994) *Photosensitive epilepsy, New Edition*. London, Mac Keith Press

Harding G, Jeavons P, Edson A (1994) Video material and epilepsy. *Epilepsia* 35(6):1208-16.

Hart EJ (1990) *Nintendo Epilepsy*. *New England Journal of Medecine*, 322, 1473 (Letter)

Hauser WA and Kurland LT (1975) The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. *Epilepsia* 16:1-66.

Helfgott P and Meister J (1983) Seizures apparently triggered by video games. *Journal of the American Medical Association* 250: 1273 (Letter)

Henchey RA and Gilmore RL (1993) Video game epilepsy following temporal lobectomy. *Electroencephalography and clinical Neurophysiology*, 86, 29P

Henner K (1963) Reflex Epileptic Mechanisms. Conceptions and experiences of a Clinical Neurologist. In Reflex Mechanisms in the Genesis of Epilepsy. Elsevier Publishing Co, Amsterdam pp 28-42

Herskowitz J, Rosman N, Geschwind N (1984) Seizures induced by singing and recitation. A unique form of reflex epilepsy in childhood. *Archives of Neurology* 41(10):1102-3.

Hume D (1739) Treatise of Human Nature. Reproduced by Selby-Bigge (Ed) Oxford, Eng. Clarendon 1896.

The Independent, United Kingdom 18/12/97

Ingvar D and Nyman G (1962) Epilepsia arithmetica: a new psychologic trigger mechanism in a case of epilepsy. *Neurology (Minneapolis)* 12:282-287.

Jallon P, Heraut L, Vanelle J (1989) Musicogenic epilepsy. In Beaumonoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies*. Geneva: Editions Medicine et Hygiene pp 269-274.

Jeavons P (1966) Summary of paper on abnormalities during photic stimulation. *Proceedings of the Electrophysiological Technologists Association* 13:153

Jeavons P, Barton M, Bishop A (1981) Seizures and hand-held space invaders. *Lancet* 2:758 (Letter)

Kasteleijn-Nolst Trenite DGA (1989) Photosensitivity in epilepsy. Electrophysiological and clinical correlates. *Acta Neurologica Scandinavica*, 80 (Suppl. 125)

Kasteleijn-Nolst Trenite DGA, Siebelink B, Berends S, van Strien J, Meinardi H (1990) Lateralised effects of subclinical epileptiform EEG discharges on scholastic performance in children. *Epilepsia* 31(6):740-6.

Kasteleijn-Nolst Trenite DGA (1994) Video-game epilepsy. *Lancet* 344:1102-1103 (Letter)

Kato K, Kan R, Takahashi R, Watabe M, Niwa S (1994) The occurrence rate of epileptic seizures during playing video games. *The Japanese Journal of Psychiatry and Neurology* 48(2):306-308.

Klinger D, Tragner H, Deisenhammer E (1991) The nature and influence of sleep deprivation on the EEG. *In Epilepsy, Sleep and Sleep Deprivation, 2nd Edn (Epilepsy Research Suppl. 2) Eds Degen R and Rodin E. Elsevier Science Publishers BV pp 231-234*

Kruta V (1963) The physiologist George Prochaska (1749-1820) and the reflex theory. *In Reflex Mechanisms in the Genesis of Epilepsy. Elsevier Publishing Co, Amsterdam pp 238-248*

Lai C-W and Trimble M (1997) Stress and epilepsy. *Journal of Epilepsy 10:177-186.*

Lau R, Bernard T, Hartman K (1989) Further explorations of common-sense representations of common illnesses. *Health Psychology 8(2):195-219*

Lazarus R and Folkman S (1984) Stress, appraisal and coping. *Springer, New York.*

Lennox W (1946) Science and seizures (2nd Edn) *Harper, New York.*

Lesser R (1985) Psychogenic seizures. *In Recent Advances in Epilepsy Vol 2. Eds Pedley T and Meldrum B. Churchill Livingstone, Edinburgh.*

Leventhal H, Meyer D, Nerenz D (1980) The common sense representations of illness danger. In Rachman S (Ed) *Medical Psychology, Vol 2. Pergamon, New York pp 7-30*

Leventhal H and Nerenz D (1985) The assessment of illness cognition. In Karoly P (Ed) *Measurement strategies in health psychology. John Wiley, New York pp 517-54*

MacMahon B and Trichopolous D (1996) *Epidemiology. Principles and Methods (2nd Edn). Little, Brown and Co., Boston*

Maeda Y, Kurokawa T, Sakamoto K, Kitamoto I, Ueda K, Tashima S (1990) Electroclinical study of video-game epilepsy. *Developmental Medicine and Child Neurology 32;493-500.*

Manford M, Fish D, Shorvon S (1996) Startle provoked epileptic seizures: features of 19 patients. *JNNP 61(2):151-156*

Matricardi M, Brincotti M, Trasatti G, Porro G (1990) Self-induced pattern-sensitive epilepsy in childhood. *Acta Paediatr Scan 79:237-40*

Mattson R, Cramer J, Collins J et al (1985) Comparison of carbamazepine, phenobarbital, phenytoin and primidone in partial and secondarily generalised tonic-clonic seizures. *New England Journal of Medicine 313;145-151.*

Mazin C and Etter M (1984) Do video games affect blood pressure? *JAMA* 252(5):626 (Letter)

Miley C and Forster F (1977) Activation of partial seizures by hyperventilation. *Archives of Neurology* 34(6):371-73.

Muskens L (1926) *Epilepsie*. Springer-Verlag, Berlin.

Mutani R, Ganga A, Agnetti V (1980) Reflex epilepsy evoked by decision making: report of a case. *Scweiz-Arc-Neurol-Neurochir-Psychiatr* 127(1): 61-7

Naquet R, Bancaud J, Bostem F, Fischer-Williams M, Gloor P, Klass D, Kugler J (1976) Activation and provocation methods in clinical neurophysiology. In Remond A (Ed) *Handbook of Electroencephalography and Clinical Neurophysiology, Vol 3*. Elseveir, Amsterdam pp 89-104

Newmark ME, Penry JK (1979) *Photosensitivity and Epilepsy: a review*. New York: Raven Press

Ogunyemi A, Gomez M, Klass D (1988) Seizures induced by exercise. *Neurology* 38:633-34.

Oller-Daurella L and Oller F-V (1989) Seizures induced by voluntary movements. In Beaumonoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies*. Geneva: Editions Medicine et Hygiene pp 139-146.

Parmar M and Machin D (1995) Survival analysis: seven practical applications. Chichester, Wiley

Penfield W and Erickson T (1941) Epilepsy and cerebral localisation. ChC Thomas, Springfield

Porter A (1985) Pattern sensitivity testing in routine EEG. *Journal Electrophysiol Technol*. 11:153-55

Pratt K, Weikers N, Mattson R, Williams R (1968) EEG activation after sleep deprivation. *EEG Journal* 24(1):11-15.

Quirk J, Fish D, Smith S, Sander J, Shorvon S and Allen P (1995a) Incidence of photosensitive epilepsy: a prospective national study. *Electroencephalography and clinical neurophysiology* 95:260-7.

Quirk J, Fish D, Smith S, Sander J, Shorvon S and Allen P (1995b) First seizures associated with playing electronic screen games: a community-based study in Great Britain. *Annals of Neurology*

Ricci S and Vigevano F (1993) Occipital seizures provoked by intermittent light stimulation: ictal and interictal findings. *Journal of Clinical Neurophysiology* 10(2):197-209.

Roger J, Leroux M, Bureau M, Dravet Ch, Santanelli P (1989) Reflex epilepsy and epilepsy with reflex seizures: study of the population of an epilepsy centre. In Beaumanoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies*. Geneva: Editions Medicine et Hygiene 463-474

Rushton N (1981) 'Space invader' epilepsy. *Lancet* 1:501(Letter)

Saenz-Lope E, Herranz-Tanarro F, Masdeu J (1985) Primary reading epilepsy. *Epilepsia* 26(6):649-56.

Sander J and Shorvon S (1987) Incidence and prevalence studies in epilepsy and their methodological problems: a review. *Journal of Neurology, Neurosurgery and Psychiatry* 50:289-39.

Schmitt B, Thun-Hohenstein L, Vontobel H, Boltshauser E (1994) Seizures induced by physical exercise: report of two cases. *Neuropediatrics* 25:51-3

Scollo-Lavizzari G, Pralle W, De La Cruz N (1975) Activation effects of sleep deprivation and sleep in seizure patients. An electroencephalographic study. *Eur. Neurology*, 13, 1-5



Scollo-Lavizzari G, Scollo-Lavizzari GR (1974) Sleep, sleep deprivation, photosensitivity, and epilepsy. *Eur. Neurology*, 11, 1-21

Segal K and Dietz W (1991) Physiologic response to playing a video game. *Am Journ Dis Child* 145:1034-6.

Senanayake N (1987) Epileptic seizures evoked by card games, draughts and similar games. *Epilepsia* 28(4):356-61.

Servit Z, Machek J, Stercova A, Dudas D, Kristof M, Cervenkova V (1962) Reflex influences in the pathogenesis of epilepsy in the light of clinical statistics. *Epilepsia* 3:315-22.

Sherwin I (1984) Hyperventilation: mode of action and application in electroencephalography. *American Journal of EEG Technologists* 24:210-11.

Siegal M, Kurzrok N, Barr W, Rowan A (1992) Game-playing epilepsy. *Epilepsia*, 33, 93-97

Stevens J (1959) Emotional activation of the electron? in patients with convulsive disorders. *JNMD* 128:339-51.

Stores G (1984) Intensive EEG monitoring in paediatrics. *Dev Med Child Neurol* 26:231-35.

The Sun, United Kingdom 18/12/97

Sutherland W, Hershman L, Miller J, Lee S (1980) Seizures induced by playing music. *Neurology* 30(9):1001-4.

Sveinbjornsdottir S and Duncan J (1993) Parietal and occipital lobe epilepsy: a review. *Epilepsia* 34:493-521

Takahashi Y, Shigematsu H, Kubota H, Inoue Y, Fujiwara T, Yagi K, Seino M (1995) Nonphotosensitive video game-induced partial seizures. *Epilepsia* 36(8):837-41.

Temkin O (1971) The falling sickness. A history of epilepsy from the Greeks to the beginnings of Modern Neurology (2nd Edn revised) *The John Hopkins University Press, Baltimore*

Thompson KJ (1993) Video game induced generalised epileptic convulsion. *New Zealand Medical Journal*, 106, 88 (Letter)

Thompson PJ (1988) Psychological aspects of non-compliance. In: Compliance in Epilepsy (Editors Schmidt and Leppik I) *Epilepsy Research (Suppl. 1):71-75*

Trimble M (1996) Psychological and psychiatric aspects of epilepsy. In Duncan J, Shorvon S, Fish D (Eds) *Clinical Epilepsy*. Churchill Livingstone, New York pp 321-348

Verduyn C, Stores G, Missen A (1988) A survey of mothers' impressions of seizure precipitants in children with epilepsy. *Epilepsia* 29(3):251-55.

Vespignani H, Huttin B, Webber M (1986) Crises epileptiques et jeux video. *Concours Medecine*, 108, 2609-12

Vidart L, Geier S (1967) Enregistrements tele-encephalographiques chez des sujets epileptiques pendant le travail. *Rev Neurol* 117:475-480.

Vizioli R (1963) The Italian contribution to the problem of reflex epilepsy. In *Reflex Mechanisms in the Genesis of Epilepsy*. Elsevier Publishing Co, Amsterdam pp 21-27

Waltz S, Christen H-J, Dooze H (1992) The different patterns of the photoparoxysmal response - a genetic study. *Electroencephalography and clinical Neurophysiology* 83:138-145.

Wiebers D, Westmoreland B, Klass D (1979) EEG activation and mathematical calculations. *Neurology* 29:1499-1503.

Wieser H, Hungerbuhler H, Siegal A, Buck A (1997) Musicogenic epilepsy: review of the literature and a case report with photon emission computed tomography. *Epilepsia* 38(2):200-7

Wilkins A, Steffanson S, Jeavons P, Harding G (1979) Television epilepsy: the role of pattern. *Electroencephalography and clinical neurophysiology* 47:163-71

Wilkins A, Zifkin B, Andermann F, McGuvern E (1982) Seizures induced by thinking. *Annals of Neurology*, 11, 608-12

Wong FS, Campbell DR, Becker BE (1983) Head injuries and video games. *Western Journal of Medecine*, 138, 107 (Letter)

Zielinski JJ (1974) Epidemiology and MedicoSocial Problems of Epilepsy in Warsaw. Final report on research program no. 19-P-58325-F-01, Warsaw: *Psychoneurological Institute*.

Zifkin B (1989) Some considerations in the intensive EEG investigation of reflex epilepsy. In Beaumanoir A, Gastaut H, Naquet R, eds. *Reflex Seizures and Reflex Epilepsies*. Geneva: Editions Medicine et Hygiene 457-462.

Zifkin B and Andermann F (1998) Complex Reflex Epilepsies. In *Epilepsy: A comprehensive textbook*. Eds Engel J Jnr and Pedley T. *Lippincott-Raven Publishers, Philadelphia*.

## Authors bibliography

### Papers

CJ Millett, DR Fish, PJ Thompson (1997) A survey of epilepsy-patient perceptions of video-game material / electronic screens and other factors as seizure precipitants. *Seizure* 6:457-9.

CJ Millett, DR Fish, PJ Thompson (1998) Photosensitivity - Better informing patients with epilepsy of their individual risk. *Seizure* 7(2):97-99.

CJ Millett, DR Fish, PJ Thompson, A Johnson. Seizures during video-game play and other common leisure pursuits in known epilepsy patients without visual sensitivity. *Epilepsia* (in press)

CJ Millett, PJ Thompson, A Johnson, DR Fish. A study of the effects of participation in structured leisure pursuits on seizure occurrence. *British Medical Journal* (submitted)

### Abstracts

CJ Millett, DR Fish and PJ Thompson (1996) Seizure rates during video game activity and other leisure pursuits in non-photosensitive chronic epilepsy patients. *Epilepsia* Vol 37 (Suppl. 5):85

CJ Millett, DR Fish & PJ Thompson (1997) Seizure rates during video game activity and other leisure pursuits in non-photosensitive chronic epilepsy patients. *Electroencephalography and Clinical Neurophysiology*

CJ Millett, DR Fish, PJ Thompson (1997) A survey of epilepsy patient perceptions of video game material / electronic screens and other factors as seizure precipitants. *Epilepsia* Vol 38 (Suppl. 3):284

Oral Presentations

CJ Millett, DR Fish, PJ Thompson. Seizure rates during video games and other leisure pursuits in non-photosensitive chronic epilepsy patients. American Epilepsy Society. 1996 Annual Meeting - San Francisco.

CJ Millett, DR Fish & PJ Thompson. Seizure rates during video game activity and other common leisure pursuits in known non-photosensitive epilepsy patients. British Society of Clinical Neurophysiologists. 1997 Annual Meeting - London.

CJ Millett, DR Fish & PJ Thompson. Seizures in non-photosensitive individuals during exposure to video games. International Commission on Electronic Screens and Seizures - Dublin June 1997

CJ Millett, DR Fish, PJ Thompson. A survey of epilepsy patient perceptions of video game material / electronic screens and other factors as seizure precipitants. 22nd International Epilepsy Congress - Dublin June 1997

**CJ Millett, DR Fish & PJ Thompson. Electronic screen game seizures. What proportion of the epilepsy population are at risk? Postgraduate Research Seminars - Institute of Neurology, London March 1998**



Appendix 1 Video games and epilepsy literature

Author	Age	Sex	Clinical History	FH	Basic EEG	Flash Sensitivity (f/s)	Pattern Sensitivity (c/deg)	VG Seizure	Video Game	Monitor	Treatment	Outcome
Rushton (1981)		17 M	Febrile Convulsion		Normal	Nil	NT					
Jeavons et al (1981)		14 M	None	NS	Left-sided spike/wave	15-18	0.38-2.7	GTC	Space Invaders	Hand-held	Valporate	
Daneshmand & Campbell (1982)		17 F	None	Nil	Normal	15-21	NT	GTC	Dark Warrior	TV	None	Seizure Free
Dalquist et al (1983)		15 M	Nil, later other PS sz	NS	Normal	15 and 20	NT	NS	Combat	TV	Valporate + Avoidance	Seizure Free
Helgott & Meister (1983)		8 M	None	Nil	Left-sided spike/wave	NT	NT	NS	NS	Arcade	Phenobarbitone	NS
Glista et al (1983)		14 M	Seizures	Nil	3-4 Hz Generalised spike/wave	Nil	NT	GTC	Intelelevision Game	TV	Avoidance	Seizure Free
		15 M	None	Nil	Normal	Nil	NT	GTC	Turbo	Arcade	Avoidance	Seizure Free
Wong et al (1983)		32 M	Head injury		Normal	NT	NT		NS	TV		
De Marco & Ghersini (1985)		8 M	None	NS	NS	10-25	NT	GTC	Space Invader	TV	NS	NS
		13 M	None	NS	Left Occipital Focal Spikes	Nil	NT	GTC	NS	TV	Carbamazepine	Two more VG seizures
Ferry et al (1986)		12 M	NS		NS	NS	NT		Chopper	NS		
Vespignani et al (1986)		19 M	Nil		Normal	Nil	NT	NS	NS	NS		
		36 F	Nil		Normal	Nil	NT	NS	NS	NS		
		19 M	Nil		NS	13-15	NT	NS	NS	NS		
Ambrosetto & Tassinari (1987)		32 M	Seizures		Normal	20	NT		NS	NS		
		16 F	Seizures		Left sharp waves	PPR	NT		NS	TV		
Giroud et al (1987)		11 M	None		Normal	15	NT		NS	NS		
		14 F	Myoclonic jerks		Normal	12	NT		NS	NS		
Hart (1990)		13 F	None	NS	NS	> 8	NT	GTC	Super Mario Bros	TV	AED treatment	NS
Maeda et al (1990)		7 M	None, later spon. sz	Nil	Occipital slow waves	3-30	PCR	NS	Super Mario Bros	TV	Valporate	Seizure Free
		10 F	None, later PS sz	Nil	Occipital slow waves	12-30	PCR		Links Adventure	TV	Valporate	Seizure Free
		12 F	None	Nil	Normal	Nil	Nil	GTC	Dream Factory	TV	Abstinence	Seizure Free
		4 M	Febrile convulsions	Nil	Normal	Nil	NT	GTC	Wrecking Crew	TV	Abstinence	Seizure Free
		12 M	None	Nil	Normal	15-30	Occipital spikes	GTC	NS	TV	Abstinence	Seizure Free
		13 M	None, later spon. sz	NS	Normal	12-30	NT	GTC	Hydride	TV	Valporate	Seizure Free
		9 M	None, later spon. sz	NS	NS	3-30	NT	GTC	Dragon Quest 2	TV	Valporate	Seizure Free
Cook & Hoskins (1992)		11 M	None	Yes	Normal	> 9	Nil	GTC	Super Mario 2	TV	NS	NS
		17 M	None	Yes	Atypical spike/wave	11-20	Nil	GTC	Super Mario 2	TV	NS	NS
Henchey & Gilmore (1993)		17 M	Seizures	NS	Rare left temp. sharp theta	Nil	NT	CPS x 3	Nintendo	TV	NS	NS
Thompson (1993)		15 M	Febrile Convulsion	NS	Normal	NS	NS	GTC	NS	Arcade	NS	Seizure free
Graf et al (1994)		14 M	Seizures	Nil	Right-sided spike/wave	9-30	NT	SP/GTC	NS	TV	Abstinence	Spontaneous seizures
		11 M	None	Nil	Left-sided spike/wave	10-30	NT	GTC	Mario Bros 3	TV	Abstinence	Spontaneous seizures
		15 F	Seizures	Nil	Spike/wave	10-20	NT	Absence	NS	TV	Ethuximide + Abst	Spontaneous seizures
		22 M	Seizures	Nil	Normal	Nil	NT	SP/GTC	NS	TV	Phenobarbitone + Abst	Seizure Free
		15 F	None	Nil	Normal	Nil	NT	GTC	Mario	TV	Phenytoin + Abst	Seizure Free
		10 M	Seizures	Nil	Right occip/posterior temp. spikes	Nil	NT	GTC	NS	TV	Valporate + Abst	TV seizure
		14 M	None	Nil	Spike/wave	15-29	NT	GTC	NS	TV	Phenytoin + Abst	Spon. + board game sz
		11 F	Seizures	Yes	Normal	Nil	NT	GTC	NS	TV	Valporate + Abst	Stroboscopic seizure
		12 M	Seizures	Nil	Spike/wave	Nil	NT	GTC	Double Dragon	TV	Carbamazepine + Abst	Spontaneous seizures
		10 M	None	Nil	Normal	Nil	NT	Absence	NS	TV	Ethuximide + Abst	Seizure Free
Harding et al (1994)		15 M	Seizures	Nil	Left spike/wave	17, 35, 50, 55	1.0-2.5	GTC	NS	TV	Valporate	VG due to non-compliance
		12 F	Non-pyrexial attack	Nil	Spike/wave	14-43	0.76-1.25	GTC	NS	TV	Valporate + CBZ	NS
		14 M	? Seizure	Nil	Normal	Nil	1.5	GTC	NS	TV	Valporate	NS
		14 M	Seizures	Nil	Spike/wave	15-50	Nil	NS	NS	TV	Valporate	NS
		15 F	Seizures	Nil	Spike/wave	11-56	0.53-5.0	NS	Terminator	TV	NS	NS
		14 M	Seizures	Nil	Spike/wave	45-55	NT		Myoclonic jerks	Atari Test Drive	TV	NS
		13 M	Photosensitive seizure	Yes	Normal	Nil	12.5	GTC	Spectrum	TV	Abstinence	NS

Appendix 1 Video games and epilepsy literature

	13 F	Seizures	Nil	Left occipital spikes	8-56	1 0-2.5	GTC	Sonic 2	TV	NS	NS
	13 M	None	Nil	Right posterior temp abnormality	Nil	1 09-3.5	GTC	Amega football	TV	NS	NS
	20 M	None	Nil	Normal	40-50	1 25-6.8	GTC	NS	Arcade	NS	NS
	12 M	None	Nil	Occipital sharp waves	12-20	1 0-6.2	GTC	Jackie Chan	TV	NS	NS
	14 F	TV seizures	Nil	NS	12-17	2 0-5.0	GTC	NS	TV	Valproate - before VGS	NS
	13 M	Photosensitive seizure	Nil	NS	45-52	Nil	GTC	Golf game	TV	Valproate	NS
Ferrie et al (1994)	14 F	Seizures	Nil	Spike/wave	15	NT	GTC	Tennis	TV	Valproate + CBZ	Seizures controlled
	12 M	Seizures	Nil	Spike/wave	Enhanced spike/wave	NT	GTC	NS	TV	Valproate	Seizures controlled
	16 M	Seizures	Nil	Spike/wave	Nil	NT	GTC	Atari	TV	Valproate + Clonazepam	Seizures controlled
	22 M	None	Nil	Normal	Nil	NT	GTC	NS	TV	Abstinence	Seizure Free
	12 M	None, other PS sz late	Yes, PS	NS	12-25.50	NT	GTC	NS	TV	Abstinence	PS seizure
	38 M	Seizures	Nil	Spike/wave	Nil	NT	Absence	Car racing	TV	Valproate + LMG	Seizures controlled
	11 M	None	Nil	Generalised sharp theta waves	Nil	NT	GTC	Super Mario Bros	Arcade	No treatment	NS
	11 F	None	Nil	Spike/wave	Yes, range not stated	NT	GTC	NS	TV	Valproate	Suppressed seizures
	12 M	Photc induced absend	Yes	Generalised discharges	> 1.5	NT	GTC	NS	TV	Valproate + CBZ	Spontaneous seizures
	11 F	Seizures	Nil	Bilateral paroxysms occipital sp	Yes, range not stated	NT	Partial	NS	TV	Valproate	Seizures controlled
	19 M	None	Nil	NS	7-27	NT	GTC	Captain Battie	Arcade	Abstinence	Seizure Free
	9 M	None	Nil	Occipital spikes	Nil	NT	GTC	Michael Jackson	Arcade	Abstinence	Seizure Free
	14 M	None	Nil	Right occipital spikes	Nil	NT	GTC	NS	Arcade	Abstinence	Seizure Free
	14 M	None	Nil	Right temp-occipital spikes	Nil	NT	GTC	Asterix V Romans	Arcade	Abstinence	Seizure Free
	15 M	None	Nil	Right temp-occipital spikes	Nil	NT	GTC	NS	Arcade	Abstinence	Seizure Free
Allen et al (1994)	13 M	None	Nil	NS	Yes, range not stated	NT	GTC	Sonic the H/hog	TV	Caution	Seizure Free
	14 M	None	Yes	Suggestive of PGE	Yes, range not stated	NT	NS	Street Fighter II	TV	Caution	Seizure Free
	13 F	PS seizures	Nil	Normal	Unstable	NT	GTC	Street Fighter	TV	Valproate + Caution	Seizure Free
								<b>Not subject matched</b>			
Kato et al (1994)	9 M	None	Nil	NS	Yes, range not stated	NT	GTC	NS	NS	Reducing exposure time	Preventative effect
	7 M	None	Nil	NS	Nil	NT	GTC	NS	NS	Reducing exposure time	Preventative effect
	11 M	None	Nil	NS	Yes, range not stated	NT	GTC	NS	NS	Reducing exposure time	Preventative effect
	13 M	None	Nil	NS	Nil	NT	GTC	NS	NS	Reducing exposure time	Preventative effect
	13 M	None	Nil	NS	Nil	NT	GTC	NS	NS	Reducing exposure time	Preventative effect
	NS	M	Seizures	Nil	NS	NT	Absence	NS	NS	Reducing exposure time	Preventative effect
	NS	M	Seizures	Nil	NS	NT	Myoclonic jerks	NS	NS	Reducing exposure time	Preventative effect
	NS	M	Seizures	Nil	NS	NT	> 2 GE seizures	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	> 2 GE seizures	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	> 2 GE seizures	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Yes	NS	NT	Simple partial seizure	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Complex partial sz	NS	NS	Reducing exposure time	Effect Unknown
	NS	F	Seizures	Yes	NS	NT	Yes, range not stated	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Yes	NS	NT	Yes, range not stated	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Complex partial sz	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Complex partial sz	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	2nd GTC	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Yes, range not stated	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Complex + other part	NS	NS	Reducing exposure time	Effect Unknown
	NS	F	Seizures	Nil	NS	NT	Yes, range not stated	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Complex + other part	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Yes, range not stated	NS	NS	Reducing exposure time	Effect Unknown
	NS	F	Seizures	Yes	NS	NT	SPS + 2nd GTC	NS	NS	Reducing exposure time	Effect Unknown
	NS	M	Seizures	Nil	NS	NT	Nil	NS	NS	Reducing exposure time	Effect Unknown
Takahashi et al (1995)	9 M	Seizures	Nil	Spike/wave	Nil	Nil	Complex partial sz	NS	Hand-held	NS	NS
Quirk et al (1995)	< 7 (1) M (85)	None (118)	Yes, PS	Normal (71)	Type 4 (46)	NT (118)	GTC (105)	NS (118)	TV (47)	NS (118)	NS (118)
	7-19 (103) F (33)		(4/118)	Generalised epileptic act (32)	Types 1-3 (16)		Absence (4)		Computer (18)		
	> 19 (14)			Lateralised epileptic act (6)	Other evidence (11)		Partial (4)		Arcade (12)		
				Single sharp wave (1)	Nil (47)		Myoclonic (2)		Hand-held (3)		
				Rolandic Spikes (1)			Uncertain (3)		Unknown (40)		
				Background abnormalities (7)							

## Appendix Two

### Questionnaire One

#### **Please Tick Only One**

Do you believe that

- (a) All people with epilepsy should not play video games because they are likely to cause seizures
- (b) Many (but not all) patients with epilepsy are at risk of having a seizure due to playing video games
- (c) A very small number of people with epilepsy are at an increased risk of having a seizure during video game play
- (d) There is **no** risk of having a seizure due to playing video games if you have epilepsy
- (e) Do not know

#### **Please Tick As Many As You Feel Appropriate**

Do any of the following precipitate a seizure for you:-

- (a) Video games
- (b) Television
- (c) Computer Screens
- (d) Flashing lights eg discotheque
- (e) Patterns of lines eg escalator
- (f) Sunlight / artificial light
- (g) Lack of sleep
- (h) Excitement
- (i) Boredom

(j) Stress

(k) None of the above

**(l) Anything else - please state**

## Appendix Three

### Questionnaire Two

Have you had an EEG before?

Were you shown flashing lights during this test?

Have you been told by your doctor that this test showed:

(a) that you were sensitive to flashing lights

(b) that you were *not* sensitive to flashing lights

OR

You were not informed of the result of this test

Have you been given any advice about being exposed to flashing lights?

Yes

No

Who gave you this advice?

eg doctor, nurse, friend

Can you briefly describe the advice that was given to you.

## **DRUG REDUCTION PROTOCOL**

**\*\* Drug reduction may help to precipitate seizures, but must be done cautiously to avoid getting non-habitual attacks or major convulsions.**

Patients who are not generally suitable for drug reduction include the following categories:-

Pregnant females

Patients with a past history of drug withdrawal status epilepticus or major injuries during drug withdrawal convulsions.

Patients with severe generalised convulsions. Such patients would be considered on an individual basis by the relevant consultant.

There is no purpose to reducing drugs with a very long half life and therefore Phenobarbitone and Primidone (Mysoline) will not be changed in terms of their dosage during the course of telemetry.

The dose of the other anticonvulsants will be halved starting at 6.00 pm onwards on the day of admission if the patient is in agreement, having had this explained to them and having given consent. In the case of Clobazam, if the patient is on one capsule at night, this will be stopped altogether.

The 6.00 pm dose on Tuesday afternoon of Carbamazepine (Tegretol) will be halved again if there have been no seizures. Similarly, the dose of Clobazam (Frisium), Diazepam (Valium), or Clonazepam (Rivotril) will be halved.

Reinstitution of drugs:- Generalised convulsion or three partial seizures within 24 hours. In that event there would be an instruction to give half the total daily dose of any drugs which have been reduced as soon as the patient became sufficiently aware and cooperative to take them orally.

NB:- Most subjects having their drugs reduced were surgery candidates in whom habitual ictal EEG recordings were necessary for confirmation of structural imaging abnormalities.

## **PARTIAL SLEEP DEPRIVATION**

This is an additional means of provoking epileptic seizures in patients undergoing telemetry. If insufficient ictal recordings have been made then suitable candidates will undergo mild sleep deprivation on either Tuesday or Wednesday night. This will involve staying up till 2.00 am and being woken at 6.00 am.

## Appendix 5 Protocol for Visual Sensitivity Testing

Testing was conducted in a darkened room

### A. Intermittent Photic Stimulation

SLE Photic Stimulator type CPS-10 with an acetate square grid was used. The lamp was placed 30cm from the nasion. An initial flash frequency of 18 Hertz followed by flash frequencies of 2,4,6,8,10,12,14,16,18,20,25 & 50 Hertz were given. A run down (50, 40, 30, 20, 10 Hertz) and a run up (1,3,5,7,9,11,13,15,17 Hertz) of flash frequencies was then instituted. In all cases, the stimulation was first given with the patient's eyes open for 5 seconds and then for a further 5 seconds after patient was asked to close their eyes.

### B. Pattern Stimulation

A standard portable X-ray viewer was covered by a 30cm square acetate with black vertical stripes of 1.5mm width spaced 1.5mm apart. The viewer was placed 40cm from the nasion. Patients were asked to close their eyes, whilst the viewer was illuminated and were then required to view the pattern for ten seconds. Exposure was given under two conditions; whilst the pattern remained stationary and when it was manually oscillated

## Use of sealed envelopes for the random allocation of Video Game and Leisure Activities

### A) Stratification

The patients entered in this study will be stratified by the day of the week (Tuesday or Wednesday) on which their activities are monitored, and whether or not they are entered as a member of a pair or individually (Pair or Single). The strata have been numbered and their characteristics are summarized in the table below.

Stratum Number	Characteristic	
	Day of Week	Pair or Single
1	Tuesday	Pair
2	Tuesday	Single
3	Wednesday	Pair
4	Wednesday	Single

Six envelopes have been provided for each stratum containing pairs, and eight envelopes for each stratum containing singles.

### B) Format of Envelopes

VGS	STR N
Stratum Characteristics	XX

The sealed envelopes for sequence allocation are buff. Each envelope carries the abbreviated study title VGS and the stratum number (prefixed STR) in blue, an abbreviated description of the stratum characteristics and a two digit serial number in red. A dummy envelope is attached to this document.



## C) Format of Cards

VGS	STR N
Stratum Characteristics	XX
STARTING ACTIVITY	
NAME: DATE:	

The randomization cards have been colour coded (stratum 1 pink; stratum 2 yellow; stratum 3 blue; and stratum 4 green), and carry the abbreviated study title (VGS), and the stratum number prefixed STR, in blue. They also have the same abbreviated stratum characteristics and the same serial number as the envelope in red. Randomization cards for patients, who are paired (strata 1 and 3), also have a letter (A or B) added to their serial numbers (in red).

The allocated starting activity appears in black in the centre of the card abbreviated as follows:

<u>Activity</u>	<u>Abbreviation</u>
Video Game	VG
Leisure	L

At the bottom of the card there are spaces for the patient's name and the date of randomization. A dummy randomization card is attached to this document.

The envelopes for strata 2 and 4 each contain just one randomization card, whereas those for strata 1 and 3 each contain TWO randomization cards. The two cards within each envelope carry the same serial number, but are distinguished by the letters A and B.

## D) Use of sealed envelopes

- (1) Activities should be allocated using the sealed envelopes only for those patients who satisfy the study entry criteria and for whom randomization is appropriate;
- (2) The envelopes should be kept and opened in **strictly increasing order of the serial numbers** in each stratum;

- (3) Only one envelope per patient should be used in strata 2 and 4. In strata 1 and 3 one envelope should be used per pair of patients. **BEFORE OPENING ENVELOPES FOR A PAIR OF PATIENTS IN STRATA 1 OR 3, ONE MEMBER OF EACH PAIR MUST BE NOMINATED AS "PATIENT A" AND THE OTHER AS "PATIENT B"**.
- (4) The envelope should be opened after the decision to randomize the starting activity has been made;
- (5) As far as possible start the sequence of activities with the activity allocated by the card;
- (6) Enter the patient's name together with the date of randomization on the card;
- (7) The cards used should be returned to MRC Biostatistics Unit; **DO NOT DESTROY THEM**;
- (8) Destroy opened envelopes.