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Photic- and Pattern-induced Seizures: A Review for the Epilepsy Foundation of America Working Group

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Summary: *Purpose:* This report summarizes background material presented to a consensus conference on visually provoked seizures, convened by the Epilepsy Foundation of America.

Methods: A comprehensive review of literature was performed.

Results: Photosensitivity, an abnormal EEG response to light or pattern stimulation, occurs in ~0.3–3% of the population. The estimated prevalence of seizures from light stimuli is ~1 per 10,000, or 1 per 4,000 individuals age 5–24 years. People with epilepsy have a 2–14% chance of having seizures precipitated by light or pattern. In the Pokemon cartoon incident in Japan, 685 children visited a hospital in reaction to red–blue flashes on broadcast television (TV). Only 24% who had a seizure during the cartoon had previously experienced a seizure. Photic or pattern stimulation can provoke seizures in predisposed individuals, but such stimulation is not known to increase the chance of subsequent epilepsy. Intensities of 0.2–1.5 million candlepower are in the range to trigger seizures. Frequencies of 15–25 Hz are most provocative, but the range is 1–65 Hz. Light–dark borders can induce pattern-sensitive seizures, and red color also is a factor. Seizures can be provoked by certain TV shows, movie screen images, video games, natural stimuli (e.g, sun on water), public displays, and many other sources.

Conclusions: Recommendations on reducing risk of seizures have been developed by agencies in the United Kingdom, Japan, and the International Telecommunications Union, affiliated with the United Nations. The Epilepsy Foundation of America has developed a consensus of medical experts and scientists on this subject, reported in an accompanying work. **Key Words:** Seizures—Epilepsy—Photosensitivity—Reflex seizures—Review.

On August 31, 2004, the Epilepsy Foundation of America held a workshop to bring together expert knowledge about photic or pattern-induced seizures (PPISs). The purpose was to begin to develop a foundation in the United States for considering how best to describe and to reduce the risk of seizures provoked by certain types of visual stimuli. A companion article (1) presents the expert consensus recommendations. This article reviews background literature on PPISs.

HISTORY OF PHOTOSENSITIVITY

Apulius is said to have reported a seizure induced by watching a potter's wheel in 125 AD (2). However, because the potter's wheel was solid at this date, the seizure could not have been due to photosensitivity from flashing spokes (3). Gowers (4) first described PPISs in 1885, with reference to a girl who had seizures when going into bright sunshine. In 1932, Radovici (5) described eyelid myoclonias and absence seizures in response to eyelid closure while looking at bright light. Livingston (6) described seizures in response to flickering on TV. General reviews can be found in several works (2,7–15).

Gastaut (16) studied 35 patients who had seizures while watching TV. They distinguished patients who had seizures from those who had fainting episodes, and those who had frequent seizures likely to be coincidentally related to watching TV. In the remainder, they believed that some relation existed to watching TV, and they documented abnormalities on the patients' EEGs. Pattern sensitivity in photosensitive subjects was first reported by Bickford and associates in 1953 (17).

PPISs from TV program content (as opposed to the flicker from the refresh rate of the raster scan of the screen) came to public awareness only gradually, on the basis of a series of publicized events. In the 1980s, frequent flashes from targets and guns in a U.S. TV show called "Captain Powers" induced a seizure in a young male viewer (18).

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In 1993, an advertisement for "Golden Wonder, Pot Noodle" was shown in the United Kingdom. This commercial used rapidly flashing contrast changes and induced three seizures on its first showing. The U.K. regulatory commission for TV (Independent Television Commission or ITC) solicited guidelines for photic stimulation on TV commercials (18). Subsequent violation of these guidelines led to 13 further known incidents of TV-induced seizures (18). The "Pocket Monster" incident in Japan, discussed later, was perhaps the most dramatic.

TYPES OF SENSITIVITY TO LIGHT

Terminology relevant to PPISs is often imprecise. Discussions may refer to photosensitivity, to seizures provoked by photic or visual pattern stimulation, to a "photomyoclonic" response with no seizures, to "photoconvulsive" or "photoparoxysmal" EEG changes in the absence of clinical manifestations, or to the development of long-term epilepsy. Each of these has different clinical significance and possibly different mechanisms. Therefore definition of terms is in order. Because no authoritative compendium exists for each of these definitions, we operationally will define our terms here.

Definitions

Photic-induced seizure: A seizure provoked by visual stimulation. The usual stimulus is a flashing light, but it can be patterns of lines, gratings, checkerboards, or other configurations.

Photoparoxysmal response (PPR): An abnormal EEG response to light or pattern, consisting of spikes, spike–waves, or intermittent slow waves. To be classified as photoparoxysmal, the spikes should not be confined to occipital regions and should not be confused with the normal visual evoked response that is phase-locked to the flash.

Photosensitivity: An abnormal response of the EEG to light or pattern stimulation, consisting of a PPR.

Photomyoclonic response: Forehead and muscle twitching in response to light flash, disappearing with eye opening. Photomyoclonic responses are most common in subjects with early alcohol withdrawal and in anxious patients. A photomyoclonic response is considered to be a myogenic component of eye flutter and not an epileptiform pattern. It is more frequently seen at low-frequency stimulation, and it disappears when the interval between stimuli is shorter than the eyelid reflex latency

Categories of EEG responses that are associated with photosensitivity

When performing routine EEGs, most laboratories measure the response to photic stimulation at flash rates from ~5 to 25 Hz. Response to patterns is not assayed, except in special situations. Kasteleijn-Nolst Trenité and colleagues (19) and Rubboli et al. (20) have recommended systematic parameters for EEG laboratories to use to test for photic or pattern sensitivity. Response to intermittent photic stimulation (IPS) is considered normal unless the response shows marked asymmetry over the two sides of the head, or spikes. Some authors grade the degree of abnormality of photic stimulation, with spikes outlasting the photic stimuli, and spikes spreading beyond parietooccipital areas graded as more abnormal. Most PPRs do not outlast the stimuli but still may correlate with epilepsy (21). Absence of photic response to IPS is normal, as is a prominent photic response, provided that it lacks spikes or asymmetry. The view of the current authors, however, is that spikes restricted to occipital regions during IPS are not currently known to have clinical significance.

A widely used EEG classification system was proposed by Waltz (22). In this scheme, class I represents occipital spikes; II, local parietooccipital spikes and biphasic slow waves; III, parietooccipital spikes and biphasic slow waves spreading to frontal regions; IV, generalized spikes or polyspikes and waves.

Jeavons and Harding (9) categorized the type of EEG response to photostimulation into three groups:

1. Responses seen only in the anterior regions (photomyoclonic);
2. Responses seen only in the posterior region (photic driving, visual evoked potentials, occipital spikes); and
3. Widespread, anterior and posterior, bilateral response (photoconvulsive).

In their experience, photomyoclonic responses were extremely rare. In distinction to the scheme of Waltz, responses in category 2 of the Jeavons and Harding classification were considered normal, including occipital spikes that did not persist or spread (23). Although occipital spikes may not be epileptiform in the Jeavons and Harding classification (which we favor), they may be useful markers for genetic studies. Category 3 photoconvulsive responses were abnormal and could be further divided into six types:

1. Spike–wave bursts, usually around three per second
2. Spike–waves at 4–7 (theta) frequencies
3. Polyspikes or polyspikes–wave
4. Spikes coinciding with the flash, but extending widely
5. Spike–waves at 3/s, lasting ≥5 s, and associated with a clinical absence
6. Bilateral, diffuse high-amplitude slow waves

Any of these patterns was sufficient for Jeavons and Harding to classify the patient as having a photoconvulsive response. Pattern 1, with 3/sec spike–waves, was most common, being seen in 88% of the photoconvulsive

studies. Jayakar and Chiappa (24) investigated characteristics of EEG PPRs. Among 3,557 patients who had EEGs at their institution, 35 (1%) patients had such responses. Most of these patients had a history of epilepsy. They found no PPRs in 48 normal subjects, which is likely a function of the small number of normal subjects surveyed, because previous literature reports of such responses in numbers ranged from 1 to 7% of patients (see discussion of Air Force studies in the epidemiology section later).

Reilly and Peters (25) found PPRs to be more likely associated with a clinical history of seizures if the spikes persisted for $\geq$100 ms after termination of the flash. Jayakar and Chiappa (24) asserted that PPRs were rare, and any such responses were likely to be associated with epilepsy. Prolonged PPRs that outlast the stimulus are more likely to be associated with epilepsy, but the relation is complex and depends on whether other epileptiform abnormalities are observed (26). Clinical correlates of EEG photosensitivity include a variety of subjective and objective phenomena, such as impaired consciousness, jerking on one or both sides of the body, eye opening and closing, and discomfort in the eyes (27). In carefully screened, asymptomatic populations, a PPR occurs in $<$1% of a sample of 100 adult subjects (28) and therefore is statistically unlikely to exceed 5%. Changes in visual fixation, rather than flashing lights, can account for some rare instances of so-called "fixation-off" epilepsy (29).

EPIDEMIOLOGY OF PHOTOSENSITIVITY

The prevalence of "photosensitivity" has been said to range from less than one in 10,000 to "5–9%" (30,31). This wide variance stems mainly from two factors: lack of clarity in what condition is being reported, and bias in referral populations. The prevalence of photosensitivity is far higher than is the prevalence of PPISs. Discussions about populations "at-risk" of a PPIS are even more problematic, because most individuals at risk will never have had an EEG, many EEGs do not adequately test for photosensitivity (32), and the value of photosensitivity in predicting an actual seizure is not known. Additionally, some individuals may have a PPIS without demonstrating photosensitivity on the EEG, because of inadequate stimuli during the EEG, medications, or chance variation.

For the most part, asymptomatic individuals do not have EEGs. Therefore any study based on patients referred to EEG laboratories will be biased toward individuals more likely to have an abnormal EEG or consist of individuals for whom EEGs are a part of a routine medical assessment, such as pilots. Among patients with certain types of epilepsy [for example, juvenile myoclonic epilepsy (JME)], the prevalence of photosensitivity can be 15–20% (33), or even higher (34). Approximately 0.7–1.0% of the world's population has diagnosed epilepsy (35), defined as seizure, in conjunction with a disorder of the brain, characterized by an enduring predisposition to generate epileptic seizures (36). An unknown number of individuals with no prior evidence of epilepsy have the potential for seizures precipitated by flashing lights. As noted earlier, large population studies on EEG photosensitivity are lacking. An exception is found in Air Force studies, in which a paroxysmal EEG abnormality is taken as a disqualification for flying aircraft. Among 13,658 men aged 17–25 years applying for Royal Air Force training, 48 (0.35%) demonstrated photoparoxysmal EEG responses (37). A Danish Air Force study (38) found a somewhat higher number of EEG abnormalities in 2.4% of 5,893 asymptomatic applicants. The abnormality consisted of interictal spikes in six (0.1%) patients and a PPR in 2.2% (38). Individuals with a PPR were denied flight training. Even though air force studies performed bulk EEG screening, the population studied was likely to be healthier than was the population at large, in that ill individuals, or those with a history of epilepsy, do not tend to apply for military flight training. Such studies also exhibit bias toward male subjects, who have a lower incidence of photosensitivity (39). Because the prevalence of photosensitivity is higher in the younger population and in people with epilepsy than in people without epilepsy, the Air Force estimates of photosensitivity are most likely underestimates.

One review of 20,000 EEGs discovered eight patients who had seizures induced by light in a natural setting, 17 with seizures that could be induced in a laboratory setting, and 225 with photoparoxysmal EEG activity only (40). This would suggest that $\sim$1.25% of individuals might have an abnormal EEG response to certain types of light stimulation, among those referred for EEGs. Another study (41) showed that 6.5% of 408 patients with a single seizure had EEG changes in response to light flash. A history of a seizure was associated with a higher risk for light sensitivity (41). Steinkruger (42) estimated that PPISs occur in one of every 10,000 people in the general population, a number at least fourfold less than the estimate of those having an abnormal EEG response to IPS.

Children are more prone than are adults to photoparoxysmal EEG changes and PPISs. Doose and Waltz (43) found PPRs in 7.6% of 662 normal children, but used "looser criteria" for an abnormal response to IPS than those used now. Eeg-Olofsson and Petersen (44,45) found that 8% of 673 normal children aged 1–15 years, and 1% of 181 individuals aged 16–21 years had an abnormal response to IPS.

The December 16, 1997, Pokemon incident in Japan provides an inadvertent "experiment-in-nature" to judge the prevalence of photic-induced seizures in a population of children. In a Pocket Monstor cartoon, a rocket-launch sequence, with flashing red, then blue screens, changing at 12.5/s for $\sim$4 s, was shown on Tokyo TV, resulting in hospital visits by 685 children (46–48). Subsequent studies

suggested that ≥560 of these children had seizures, although some had migraines, visual distortions, nausea and motion sickness, or other nonseizure symptoms. Approximately three fourths of the children had no history of epilepsy (49), and more than half the children who had experienced a previous convulsion had a history of a seizure induced by TV (50). Given that ~7 million children were watching the children's program, this suggests that roughly 1 in 10,000 children had a seizure in response to this photic stimulation. This figure is probably an underestimate of the total population of pediatric patients able to have seizures in response to visual stimulation, because some might have been sensitive to other frequencies of stimulation or to patterns of light. Conversely, photosensitivity is less common in adults, so the estimate of 1 in 10,000 would overestimate the global population figure. The incidence estimated from the Pokemon incident thus is remarkably similar to that obtained by Quirk et al. (51) in a study based on EEG laboratory surveys in the United Kingdom (see later).

Genetics plays a role in tendency to develop PPISs. Waltz (23) in Germany performed family studies of 41 patients with PPISs. In this study, 50% of siblings with one photosensitive parent were themselves photosensitive, suggesting a dominant mode of inheritance of the tendency. A 1989 study (52) found that a family history of PPISs was present in 14% of 2,053 patients seen in a seizure clinic with any type of seizure. Takahashi (53) performed EEGs on 21 siblings of 17 patients with PPRs. Generalized paroxysmal EEG discharges occurred in 24% of the siblings. The prevalence and incidence of photosensitivity vary with age, being higher in the young. Onset of PPISs usually arises at age 12–15 years (9,52).

In Great Britain, the annual incidence of new-onset seizures due to unequivocal photosensitivity was 1.1/100,000 in the overall population, but 5.7/100,000 in the age range 7–19 years (54). PPISs occur in 1/4,000 individuals between ages 5 and 24 years. Photosensitivity and photic-induced seizures usually manifest around puberty, and 90% of patients with PPISs have an initial seizure before age 20 years (18). However, it is an oversimplification to state that individuals grow out of photosensitivity. Harding and associates (55) and Jeavons et al. (39) demonstrated that approximately two thirds of 100 people with photosensitivity continued to show photosensitivity on the EEG, and in some instances, continued to have photic-induced seizures, for a mean of 14 years after the initial diagnosis. In contrast, photosensitivity disappeared over long-term follow-up in 25 of 42 photosensitive patients (56). Scott and Elian (57) explicitly studied PPRs in 52 patients older than 30 years, demonstrating that photosensitive responses can be identified in adults.

Female-to-male ratio for photosensitivity ranges from 1.5 to 2.0 (18,39,58). However, males predominate among video game–induced seizures, because many more boys than girls play such games. Racial or ethnic background may make a difference in incidence of photosensitivity. In Africa, photosensitive EEG responses were seen in 2.5% of the white, 1.3% of the mixed race, and in 0.9% of the African population subgroups (59). Among adult Arab seizure patients, 24 (7.3%) of 327 showed EEG spikes to light flash (60).

A PPIS does not require a prior diagnosis of epilepsy; for many individuals who have such a seizure, it is their first seizure. The prevalence of photic or pattern-induced abnormal EEG discharges is higher for those known to have epilepsy. Among people presenting with new-onset epilepsy, ~2% have PPISs (51). People with primary generalized epilepsies are more likely than those with partial epilepsies to be sensitive to light, although any type of seizure can be associated with light sensitivity. In a group of 61 children with JME (age range, 7–16 years), 90% were photosensitive, defined as a generalized spike or spike–wave occurring at least twice during photic stimulation (34).

Photoconvulsive seizures are most common with generalized processes, including acute alcohol withdrawal syndromes (61) and idiopathic generalized epilepsy (62). However, partial seizures also can be provoked by flashing lights or patterns. Among 80 patients demonstrating some form of PPIS (52), precipitants comprised TV in 48% and sunlight or electric lights in 7%. Apparently generalized tonic–clonic seizures were seen in 44% and secondarily generalized seizures in 35% (52). The prevalence of focal seizures among those with photic-induced seizures ranges from 2.8% (3) to 29% (10), and as high in some studies as 60% (63). Most of these focal seizures were spontaneous, not photic induced. Focal paroxysmal responses in the EEG have been correlated with focal seizures, and generalized PPRs with generalized seizures (64). Most individuals with reported video game–induced seizures have PPRs in EEG testing, but some do not (65).

Photosensitivity is stable over intervals of days in a given individual, if allowances are made for circadian (time-of-day) variation (66). This stability allows EEG measures of photosensitivity to be useful for screening of antiepileptic drugs (AEDs) as a model for testing AEDs (66). In such screening, the acute suppression of photosensitivity serves as evidence of antiepileptic action but not of long-term efficacy for treatment of photosensitive epilepsy.

Concurrent conditions may predispose certain individuals to photoconvulsive attacks while viewing a screen. Such factors include alcohol withdrawal (67) and sleep deprivation (68). Among patients with epilepsy, ~2–5% can have seizures precipitated by watching TV (9,69), but not every study has found a high prevalence of TV sensitivity in patients with photosensitivity (70).

What is the incidence of seizures precipitated by video games? No definitive answer to this question is yet

available. A 3-month Department of Trade and Industry study involving 118 patients (51,54) surveyed about "90%" of all EEG departments in Great Britain over a 3-month time during 1993 through 1994, for all patients having seizures with photosensitivity, and all people whose presenting seizure occurred while playing an electronic screen game, whether or not they were photosensitive on the EEG. Seizures were categorized by direct review according to the criteria of Waltz (see earlier). Type 4 responses (generalized spike–waves) were most closely associated with a tendency toward seizures.

Patients were divided into group A: seizure definitely considered to have been triggered by playing the screen game, including a requirement for type IV photosensitivity. Group B were probable cases; group C were people with seizures unlikely to be related to the screen game. Among the group A definite cases, 43 of 46 had the presenting seizure while playing the electronic game, and three of 46, within 10 minutes of finishing a session. Among the 25 group B cases who were classified as probable (mostly because they had type 1–3 EEG photosensitivity), 22 of 25 had a seizure while playing, and three of 25 within 10 min of finishing. Most of the seizures occurred within 30 min of starting play. An estimated annual incidence of an initial seizure triggered by a video game was 1.2 per 100,000, and 5.7 per 100,000 among children from 7 to 19 years old. This can be compared with an overall incidence of new cases of seizures of all types of 55 per 100,000 in this age group. Precipitating factors were evenly divided between broadcast TV and electronic screen games, although more hours were spent watching TV. Sleep deprivation was an associated factor. Possible inaccuracies in the estimates discussed by the authors derived from the likelihood that not every individual with PPISs was captured (particularly if a seizure was mild), and not every EEG identified photosensitivity. This study remains one of the very few population studies of seizures induced by light stimulation.

Seizures induced by patterns occur with an incidence of ~30% of flash-sensitive patients in the case of stationary patterns, and ~70% for vibrating patterns (14). Individual patients may have sensitivity to flash, to certain patterns, or to both. Patterns particularly likely to produce either an abnormal EEG response or a seizure in susceptible individuals include lines or gratings, especially in an oscillating motion (71–74); however, a wide variety of patterns can provoke seizures in particular patients.

MECHANISMS OF PHOTOSENSITIVITY

Why does a light flash induce a seizure? Only partial answers are available. Cellular mechanisms are difficult to study in patients because of ethical and practical constraints. Animal models of photic-induced seizures are available [for example, photic-sensitive chickens (75) or light-sensitive baboons (76)]. If a seizure-producing drug is applied in low concentration to the visual cortex of a rabbit, then a continuous progression can be seen from normal visual evoked potentials to light flash and epileptiform spikes evoked by light flash, as the epilepsy develops (77). However, the extent to which findings in these models predict or explain human epilepsy is unknown. It would be very useful to have a validated animal model as a screening tool for visual stimuli.

Seizures involve synchronization of large networks of brain cells, so that the cells fire in unison during a seizure. EEG during a seizure reflects summed synchronous activity of millions of brain cells. During normal awake brain activity, cells fire in independent patterns, and EEG remains low voltage. Photic abnormalities in cortex probably arise from mechanisms that process visual information, and these may be quite normal. Photosensitivity can occur in patients whose vision is normal, not only as regards acuity, but also as regards the ability to see low-contrast gratings that would, at higher contrasts, elicit seizures (14). Wilkins (14,78) pointed out that the visual stimuli that provoke seizures are "strong" stimuli in that they (a) have low thresholds; (b) interfere with (or mask) the perception of other target stimuli; (c) are able to trigger relatively high amplitude visual evoked potentials; and (d) result in relatively high cerebral blood oxygenation. Meldrum and Wilkins (79), on the basis of pharmacologic evidence, postulated a diffuse insufficiency of γ-aminobutyric acid (GABA)ergic inhibition as one possible mechanism for photosensitivity. Pyramidal cells share inhibitory processes, and when strong stimuli result in a high level of excitation in pyramidal neurons, these shared inhibitory processes are compromised, resulting in a spread of excitation. A sudden sensory stimulus can engage sensory regions of brain and cause brain cells in that region to act in unison.

Binnie et al. (71) showed that gratings that drift continuously toward the center of gaze are not provocative for epileptiform discharges, although those that move with the same velocity but repeatedly change their direction of movement or phase (black–white; white–black) can be highly provocative. Stationary gratings pose a risk somewhere between these two extremes. Wilkins and colleagues (80) argued that the contours from drifting gratings move into and out of the overlapping receptive fields of cortical neurons, providing a sustained level of firing but without any temporal synchrony. Gratings that repeatedly change direction of movement cause a synchronous change in the population of neurons firing by virtue of the direction selectivity of the receptive fields. Similarly, gratings that change their phase also synchronize the firing of large numbers of cells. It is presumably when excessive numbers of cells are acting in concert ("hypersynchrony") that inhibitory mechanisms can be insufficient to meet

demand, and the synchronized firing spreads. Limited regions of synchrony can produce EEG changes (photoconvulsive or PPR) with no behavioral seizures.

The visual cortex is located in the occipital lobe of the brain. The most posterior part of the visual cortex is sensitive to light, more anteriorly to edges, and even more anteriorly to moving or changing edges and other complex geometric patterns (81,82). Individual brain cells respond to edges in particular orientations, with some cells being excited by a given pattern, and others inhibited. Thus a visual stimulus selectively activates certain regions of brain containing cells "tuned" to respond to the characteristics of that stimulus. In a series of psychophysical studies of the EEG response to pattern in photosensitive patients, Wilkins and colleagues (14) showed how the response varies with the line length within the pattern, the angular subtense of the pattern, its spatial frequency, duty cycle, luminance, and contrast. The response is greater when the image is fused in binocular vision, indicating binocular interaction, one of several lines of evidence indicating a trigger in the visual cortex. From a series of inferences, they conclude that seizures begin when normal physiologic excitation in the occipital cortex exceeds a critical amount. Stimulation in the central visual field is as effective as that in the periphery when cortical magnification is taken into account. Although large areas of the visual cortex appear to be equipotential for evoking seizures, the seizure threshold in one cerebral hemisphere can differ markedly from that in the other, even in patients with primary generalized epilepsy.

The normal response to a light flash or reversal of black–white edges is a synchronous firing of neurons in the visual cortex. This can be measured with computer EEG-enhancement techniques in normal individuals and is called the "visual evoked potential" or the "visual evoked response." Patients with PPISs tend to have enhanced visual evoked potentials to light flash or checkerboard (16,83). Porciatti and colleagues (83) showed that the increase in the size of the evoked potential with increasing contrast is abnormal in photosensitive patients at high contrasts, which is consistent with the earlier hypothesis that the seizures are triggered when normal physiologic excitation exceeds a critical level as a result of a failure of shared inhibitory processes. Dopaminergic mechanisms may be particularly important in photosensitivity (84).

Common wisdom has held that photoconvulsive attacks begin by affecting the occipital lobe, the region of brain processing of visual information. However, discharges in the photosensitive baboon, *Papio papio*, often begin frontally in the region of motor cortex (76,85), for reasons that appear to involve periocular afferents. Occasional patients also appear to have EEG frontal origin of seizures in response to visual stimuli, for equally obscure reasons, although in others, a progression from posterior to frontal regions can be seen. A study by Matsuoka (86) of the children in Japan with PPISs and five patients with reflex writing seizures was done to investigate the region of EEG onset of seizures. The photic induction was performed by red flickering light at 20 cd/m^2. Seizures tended to begin in the occipital region and spread anteriorly. Takasaka and colleagues (87) used computer measurements of coherence between different EEG channels to determine where PPISs began. In patients with predominantly occipital discharges, the occipital EEG leads paced discharges elsewhere. However, for patients with generalized photosensitive EEG patterns, frontal leads appeared to lead the discharges.

Studies using magnetoencephalography (MEG) (88) documented enhancement of phase synchrony in the gamma-band (30–120 Hz), harmonically related to the frequency of photic stimulation, and preceding the PPRs. Their findings were consistent with the idea that normal synchronized activity of large numbers of cells brought about by repetitive visual stimulation (evidenced by the harmonic gamma activity) results in a failure of inhibitory processes and culminates in the pathologic synchronization of the epileptic discharge. MEG was used by Inoue and associates (89) to investigate localization of electronic screen game–induced spikes. Patients who were photosensitive had MEG-documented posterior predominance of source dipoles in patients who had spikes during electronic screen games (89), but additional dipoles were localized to the supplementary motor area, perisylvian region, and medial temporal lobe.

Functional magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (90) showed elevated lactate levels in occipital cortex in the resting state and increased visual cortex activation with photic stimulation. Other altered areas included motor cortex and posterior cingulate gyrus in the medial frontal region between the hemispheres. Positron emission tomography (PET) studies with oxygen-15 (91) showed that statistically significant increases in regional cerebral blood flow occurred in occipital cortex, Brodmann's areas 17, 18, 19, hypothalamus, caudate, hippocampus, and scattered other regions.

When visual stimuli are restricted to one portion of the visual field (left–right, superior–inferior), the evoked EEG response tends to be maximal in the part of the occipital lobe responsible for processing that part of the visual field (92). The likelihood of generating a photosensitive response in a susceptible individual appears proportional to the amount of visual cortex activated in either hemisphere by a suitable stimulus (14,78). Although occipital lobe is the key structure in generation of PPISs, occasional patients with complex partial seizures that can be triggered by light flash can be cured by a standard temporal lobectomy (93). In properly localized cases, complex partial seizures triggered by light may respond to temporal lobectomy even when photic spikes continue in the occipital lobe (94). This suggests surgical interruption of

a seizure propagation pathway, or that a "critical mass" of synchronized neural activity is necessary for a seizure.

Evidence is substantial from animal models and clinical experience to support the concept that photic or pattern stimuli can induce seizures in susceptible individuals. However, no evidence suggests that photic or pattern stimulation leads to epilepsy, the condition of spontaneously and chronically recurrent seizures.

CHARACTERISTICS OF THE STIMULI

Characteristics of flickering stimuli that influence the likelihood of provoking a seizure are listed in the monograph by Jeavons and Harding (9), and the characteristics of patterned stimuli, in the monograph by Wilkins (14). These include intensity, duration, distance from the source, background illumination, diffusion of the pattern, contrast, type of pattern, color, open versus closed eyes, one- versus two-eye viewing, and stage of sleep–wakefulness cycle.

Whether an individual is found to be sensitive to light or pattern will depend on how the patient is tested in the EEG laboratory. Different laboratories use different protocols to perform EEGs. Some do not perform any photic stimulation as part of the routine EEG, and few use visual patterns as part of the routine EEG. In 1996, a group met in the Netherlands to establish consensus on methods for testing for photosensitivity (32). Characteristics of stimulators similar to that of the Grass photostimulator were specified. EEG was recommended to include a common reference montage of $\geq$16 channels distributed around the head. The subject should be positioned with eyes (or nasion) $\geq$0.3 m from the photic stimulator with dim surrounding illumination. Flashes should be delivered in separate trains of 10 s for each frequency with intervals of 7 s minimum. Subject's eyes should be open initially, and then closed after 5 s until the stimulation ceases. Testing frequency should include 1, 2, 3, 4, 6, 8, 10, 12, 14, 16, 18, and 20 flashes per second. A second sequence should begin at 60 Hz and decrease through 50, 40, 30, 25, and 20 flashes per second. The stimulation should be stopped if epileptiform discharges are observed. The stimulation procedure should last a maximum of 6 min. The electroencephalographer should be aware that repeating a frequency can lead either to potentiation (increase) or habituation (decrease) of the PPR (95).

Brightness, contrast, and size

The few studies that have addressed the issue agree that seizures from light stimulation are more likely with bright light than with dim light (96,97). A variety of different units and measurements for brightness are used. A difficulty with measurement arises because the flashes from conventional xenon discharge lamps are intensely bright, but very brief. Stroboscopes designed to induce EEG abnormalities recorded in the laboratory can deliver flashes with durations of 10 ms and 400,000–1.5 million candlepower at 2 feet (98). This is equivalent to 1.44 joules, or, more meaningfully, 22 lumen s/foot-squared. At 1 (lumen s) per (foot squared) = 10.764 s cd/m^2, this is equivalent to 237 cd/m^2, which compares with 100–200 cd/m^2 for conventional TVs. High-contrast stimuli are more likely to provoke seizures than are bright lights against a light background (97), within variable individual susceptibility to brightness (99). Spreading light more diffusely over the visual field increases the risk for induced seizures, provided that luminance is kept constant (100). Chatrian and associates (72,98) studied four patients with pattern-sensitive seizures. Monocular stimuli tend to be ineffective in provoking seizures (72,98). The effect of luminance on producing seizures is described in a sigmoid curve. At very low (scotopic) light levels, little effect is found; over the mesopic range, a very steep effect of increasing luminosity is seen; and then above a maximum threshold, well into the photopic levels, the curve flattens out once again. Patterns confined to the periphery of the visual field can provoke epileptiform EEG activity, provided they project to a sufficient area of the visual cortex (14).

Flash rates

Repetition rate of flash or pattern is second only to brightness in its influence over PPISs. The repetition range to provoke seizures usually lies between 15 and 25 cycles per second, but for some patients, the upper limit of sensitivity can be as high as 65 cycles per second (9). Flashes at rates $\leq$45 cycles per second can evoke EEG discharges and myoclonus (101). A rare patient will have seizures in response to single bright flashes. One patient could produce seizures and EEG changes by mental imagery of flash (102), and another by eye-blinks alone, in the absence of measurable photosensitivity (103).

Figure 1 (adapted from ref. 18) shows the distribution of the percentage of people with a photoparoxysmal EEG response to IPS at different flash rates. A broad peak can be seen at 12–30 flashes per second. The mains frequency is 60 Hz in the United States and 50 Hz in Europe;

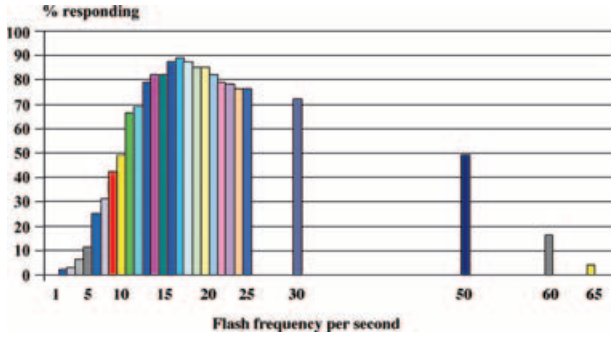

FIG. 1. Histogram depicting the percentage of known photosensitive subjects who show EEG photosensitive responses at particular flash frequencies. Adapted from Harding and Harding, 1999 (18).

fluorescent lights flash at twice the mains frequency. In Japan, both 100 and 120 Hz are used in different regions. However, when the bulbs become old, the flashes may not be equal intensity, and the lamps may emit flicker with frequency components at values significant for PPISs. Binnie and associates (104) studied 20 patients found to be photosensitive on routine EEG investigation, by exposure to fluorescent lights. No patient was sensitive to normal fluorescent lighting, but some were minimally sensitive when the lamp was defective and emitted 50-Hz flicker. Fluorescent lights were not thought by these authors to be a major public risk factor for photic seizures, although some photosensitive patients do complain of (normally functioning) fluorescent lighting.

Color

Red-colored flicker, at wavelengths of 660–720 nm, is more likely to provoke seizures than is blue or white of the same overall intensity (105,106), although some studies (107) have disputed that color makes a major difference. Sensitivity to color depends on the type of epilepsy (108), such that with myoclonic epilepsies, brightness is a key factor, but with symptomatic generalized and localization-related epilepsies, color is an important factor. Individual differences in the effects of colored light may cause some patients to benefit from spectral filters that in other patients would exacerbate their sensitivity (109).

Patterns

A surprisingly high proportion of photosensitive patients are sensitive not only to flicker but also to patterns, as first documented by Stefansson et al. (74,110). The proportion sensitive to both forms of stimulation depends on their spatial and temporal characteristics. Using patterns on a TV monitor, Harding and Jeavons (3) found that 30% of photosensitive patients also were pattern sensitive. Parallel lines or stripes are more seizure provoking than are wavy lines or polka-dot patterns. Visual angles separating lines were most seizure provoking at 4–40 min of an arc (60 min is 1 degree; i.e., the sensitivity is maximal at ~3 cycles per degree). Both horizontal and vertical patterns could induce seizures, and a given individual may be more or less sensitive to a particular orientation (72,74,111).

Oscillating gratings at 15–25 per second (7.5 degrees/s drift velocity), or 2 to 4 cycles per degree, can be a potent stimulus for seizures in some individuals (14,71,112,113). If the movement is perpendicular to the lines of the pattern and repeatedly changes direction, so as to vibrate the pattern at a frequency close to 20 Hz, the movement is extremely provocative for seizures. If the movement is continuous in one direction, then the pattern is almost without effect (71).

Wilkins et al. (114) summarized characteristics of patterns likely to provoke seizures in pattern-sensitive individuals. Stationary, oscillating stripes or black–white reversals tend to evoke pattern-sensitive discharges; whereas slow drift of lines in one direction does not. Striped patterns subtending ~2 degrees are more provocative; as stripes increase in size, their spatial frequency decreases, and fewer stripes appear on the screen. The effects of the two parameters, change in size and change in spatial frequency, oppose each other. On a TV screen viewed from conventional distances (at which it subtends ~10 degrees at the eye), a stationary pattern with no more than eight light–dark stripe pairs is unlikely to produce seizures at any size on the screen. An oscillating or alternating pattern is has equivalent risk when it has no more than five stripe pairs. Furthermore, seizures rarely are provoked by patterns occupying <25% of a screen or lasting for less than half a second.

In real life, a wide variety of stimuli can provoke photic-induced seizures. Newmark and Penry (2) listed TV, lightning, car headlights, automobile riding or driving, flickering arc light, patterns of sunlight, red-and-white checked tablecloths, sudden appearance of the sun or bright light, flickering light or sunlight (interrupted light rather than light flash), helicopter blades, walking by a picket fence, reflections on a wall, reflections on snow or water, home movies, amusement arcades, discotheques, and seizures self-induced by blinking in bright light or by waving outstretched fingers across the eyes. To this list, we also add cathode-ray tubes, video display tubes, computer monitors, decorative lighting, banner advertisements, public events with stroboscopic lighting, and video games.

Other stimulus characteristics

Patients may avoid seizures by covering one eye with the palm of a hand, provided they have sufficient warning of the seizure onset. However, closing the eyes is not necessarily effective and may even be counterproductive because the light diffuses through the closed eyelids, and the area of retina stimulated with flicker thereby may be increased (9). The opposite phenomenon also may be observed: some children self-induce PPISs by blinking, attempting to close their eyelids against the upward deviation of their eyes (which induces eyelid tremor), head-nodding, waving their outstretched fingers in front of their eyes, or intentionally looking at striped patterns (10,115–117). Studies have shown that from 10% (118) to ~33% of the photosensitive children (116) could self-induce seizures by self-inducing flicker.

SEIZURES FROM TELEVISION

In 1975, Jeavons and Harding (9) reported their widely cited study on 454 patients with epilepsy and EEG photosensitivity. Among these, 35% had seizures provoked only while watching TV, 5% had seizures while watching TV or while exposed to other environmental flashing lights, but not spontaneously, and 22% had seizures both spontaneously and while watching TV.

In the United States and Japan, TV screens scan at 60 Hz (National Television Standards Committee, NTSC standard), but an interlaced double linear raster pattern flickers at 30 Hz, and can be resolved when the viewer is close to the screen. TVs trace ~625 lines on the screen, roughly half of the lines drawn on one scan from top to bottom, and the remaining half on the next. The two scans of odd-numbered and even-numbered lines alternate continuously to provide 30-per-second visual stimulation. In Europe (Phase alternating line, PAL standard), the numbers are 50 Hz and 25 lines/s, respectively. The frequency range of 15–25 per second is among the most common frequency range for inducing photic seizures. Because stimulation at 50 flashes/s produces PPRs in 49% of photosensitive patients, whereas only 15% of patients are sensitive to 60 flashes/s, European TV is more likely to induce seizures than is American TV (117). However, factors that may alter this estimate include visual acuity of the watcher, uniformity of the TV image, refresh frequency of the screen, ambient lighting in the room, and brightness of the screen, among others.

Early studies (110) documented the association of pattern-sensitive seizures with horizontal or vertical scan lines on standard (British) TVs. TV characteristics most likely to provoke seizures were frequency of the TV screen (50 Hz was more provocative than was 100 Hz, the distance from the screen (0.5 m was more provocative than 1 m), and the specific pattern of the images (119–121). Video display units (VDUs) should be less likely than TVs to provoke seizures, because VDUs tend to be smaller, less bright, usually refresh at 70 Hz, as opposed to 50 or 60 Hz, and they do not have the interlaced double raster scan that provides a flicker at half of the scan frequency (113). However, video display computer screens still can produce photic seizures in the sensitive subject (113). A PPR is to be expected among most patients who have a seizure while watching TV. Among 13 patients having a seizure to the Pocket Monster cartoon, 12 had a photoparoxysmal EEG response (122).

STUDIES OF VIDEO GAMES

In 1981 Rushton (123) wrote a letter to *The Lancet* about "Space invader epilepsy." A near-simultaneous report was filed by Jeavons and colleagues of seizures provoked by a hand-held video game (124). This was followed by a report in England of seizures during the video game "Dark Warrior" (125). Several other cases were reported from Europe. The first case in the United States of seizures associated with video games was reported by Dahlquist and associates (126). A death of a 14-year-old boy in the United Kingdom in 1992 precipitated media coverage (127) and plans for a conference on the issue, held in London in 1993 (128). In 1994, Ferrie (68) reviewed 15 patients who experienced seizures while playing video games, discussed these in the context of 20 previously published cases in the English literature, and coined the inaccurate term "video game epilepsy." In Ferrie's review, 27 of 35 cases experienced their first seizure while playing a video game, emphasizing the difficulty of predicting risk factors in the general population. About two thirds of these patients had idiopathic generalized epilepsy with tonic–clonic seizures and somewhat typical myoclonic jerks during video games. Of the group with idiopathic generalized epilepsy, 70% were photosensitive to IPS during recording of the EEG. The term video game epilepsy is inaccurate in two ways: first, the games provoke seizures but are not known to cause epilepsy; and second, these seizures are not specific in most cases to video games.

Video game–induced seizures subsequently have been reported in a total of 553 subjects (51,54,59,119,129–133), although some subjects might have been represented in more than one study. The largest study in this area was that of Kasteleijn-Nolst Trenité and colleagues (131), who united five study sites in four European countries to collect information on patients with video game–related seizures. In total, 387 patients were studied: 75% female and 55% younger than 18 years. In the EEG laboratory, photic stimulation, pattern stimulation, viewing of TV, and playing of certain video games were performed. Photic stimulation produced epileptiform discharges in 85%, 50-Hz TV in 45%, and pattern presentation in 28%. In the study of Graf et al. (59), seizures tended to occur in association with high-intensity, repetitive flashes or rapid movements across the screen, rapid scene changes, and linear patterns rolling or flickering across the screen. Internal psychological characteristics, such as mental calculations (134) or sustained attention (135), or changes in pattern but not light flashes (130) can induce seizures in rare cases.

It can be difficult to decide whether a seizure was provoked by a video game. Seizures occur spontaneously and in coincidence with a variety of proceeding stimuli. A community-based study in the United Kingdom by Quirk et al. (51) was performed on 118 patients reported to have had a seizure within 10 min of playing an electronic screen game. Patients were captured through reports from a consortium of 118 EEG Departments, representing ~90% of the EEGs done on seizure patients in Great Britain. They classified the 118 patients with presumed seizures in association with electronic screen games into three groups: A (definite), with the seizure triggered by playing the game; B (probable), with the seizure probably triggered by the game; and C (unlikely), with probable chance association. Their group divided into 46 in A, 25 in B, 47 in C. Therefore ~40% definitely had a game-provoked seizure, ~20% may have had a game-provoked seizure, and ~40% had seizures only coincidentally related to the game.

William et al. (136) recommended three criteria to associate a seizure with a video game:

1. Repeated occurrence of seizures while playing video games;
2. History of photosensitivity with epileptiform activity triggered by other visual stimuli; and
3. EEG demonstration of PPR including two during video game playing.

According to the National Survey of Photosensitivity and Seizures Induced by Electronic Screen Games of the Institute of Neurology, London (51), most of the seizures occurred within the first 30 min of playing, but some were delayed, and some occurred within a matter of seconds. However, the seizure may be a first seizure, with no prior association with photic stimuli and occasionally no EEG findings. Should such a first seizure occurring while playing a video game be excluded? No clear answer exists, but most authors have considered a seizure occurring during a video game to be precipitated by the video game. Seizures occurring more than a few minutes after cessation of a video game are of questionable relation, but still may reflect some, as yet poorly understood persistent brain hyperexcitability.

An occasional patient with a video game–provoked seizure may have no response in the EEG to IPS, although this is an exception (73).

Different video games have variations in brightness from scene to scene. Ricci and Vigevano (136) identified four categories of video game factors responsible for triggering seizures: (a) patient-dependent factors (the internal sensitivity of the patient to flicker, pattern, etc.); (b) screen-dependent factors (size, flicker frequency, number of scan lines, refresh rate, brightness, contrast); (c) image-dependent factors (brightness, contrast, lines, colors, flashing, moving patterns); (d) software-dependent (opportunities for the player to move a joystick, change the program or interact). Review of 12 video game programs in 30 subjects suggested that a "steady maximal brightness" >100 lux was a key factor and could (in the presence of other stimuli characteristics) induce seizures in susceptible patients (137). We note, parenthetically, that lux is a measure of illuminance, rather than luminance, so this might more usefully have been expressed in candela per meter squared of luminance. Steady maximal brightness <50 was generally safe. By comparison, steady maximal brightness varied from 6 and 305 lux among the games.

Can individuals with epilepsy, but with no known photoparoxysmal sensitivity, safely play video games? This question was investigated by Millett and colleagues (138) in the study of 212 patients with epilepsy, all lacking photoparoxysmal or pattern sensitivity abnormalities during EEG testing. Patients were randomly assigned to a video game–playing session or to other leisure activities. They then crossed over groups, while undergoing video-EEG monitoring. End point was a clinical seizure. Twenty-five patients experienced a seizure while participating, 13 during video game play and 12 during other leisure activities. No support was seen for prohibiting video games in the ≥95% group of patients with epilepsy who do not give evidence of photosensitivity.

Findings similar to those of Millett et al. (138) were presented in abstract form by one of the current authors (Ledin K, Fisher RS, unpublished data). The investigators studied 46 patients playing video games, compared with the same time of day 24 h later, when not playing a video game. A total of 20 of the 46 patients had seizures: six while playing video games and 14 during the control period. None of the subjects had an abnormal PPR, and only two had primary generalized seizures. No evidence was found to justify prohibition of video game playing in patients with partial seizures and no evidence of EEG photosensitivity.

The relative safety of playing video games for the majority of seizure patients is not uniformly recognized by people with epilepsy. A survey by Millett et al. (139) in the United Kingdom found that one of 13 patients in a seizure clinic believed that every individual with epilepsy was at risk of a seizure from video games, and risk estimation by the patient population was 2–3 times the realistic risk.

RECOMMENDATIONS IN THE LITERATURE

Multiple authors and several convened groups have formulated recommendations for people with PPISs, for manufacturers of devices that might provoke photic- or pattern-induced seizures, and for governmental regulatory bodies. No one agency speaks authoritatively on this subject, although the International Standards Organization is in the process of issuing a summary of its workshop. Relatively little discussion of photosensitivity has taken place in the United States.

Ferrie et al. (68) recommended that patients who have experienced a video game–induced seizure may be allowed to continue playing in some circumstances. Play should be stopped in the presence of absences, jerking, or unusual visual phenomena. Photosensitive patients should avoid black-and-white checkered floor tiles or patterns, stripes, light through window vents, rotating ceiling fans, flashing lights, and sitting <3 m from a TV. Funatsuka and colleagues (113) recommended that pattern-sensitive individuals avoid the following: (a) geometric patterns, especially stripes occupying much of the display; (b) fine patterns with spatial frequencies >2 cycles/degree; (c) frequencies ~20 Hz with pattern-reversal stimulation; (d) patterns with large differences in brightness; and (e) rapid pattern movements. The National Association of Commercial Broadcasters in Japan and Nippon Hoso Kyokai made recommendations for producers of animated programs. They suggested that flickering, especially red

flickering at more than three per second, should be avoided. Reversing of contrasting images and rapid conversion of images should be no faster than three per second. Stripes, whorls, and concentric circles should not occupy a large part of the screen.

In their major monograph, Harding and Jeavons (3) made six recommendations for precautions to be taken by people who are sensitive to flickering lights. These were as follows:

1. View TV from ≥8 feet;
2. View in a well-lit room with a small lamp on top of the TV set;
3. Do not approach the TV set to adjust or switch channels;
4. Cover one eye if it is necessary to go near the TV;
5. Avoid discotheques or places with flashing lights; and
6. Wear polarized glasses on sunny days to reduce flickering reflections from water, etc.

SCREENING DEVICES

Risks pertaining to photosensitivity can be reduced in several ways. One approach is to prevent the promulgation of seizure-provocative video material, and the second is to prevent individual patients from being exposed to such material.

Preventing provocative image sequences

The widespread use of video material that can cause seizures arises because the material is eye-catching and can be attractive to individuals whose health is not affected, and indeed to a few who are seizure prone. Guidelines preventing the broadcast of hazardous video sequences have been in place in the United Kingdom and Japan since 1994 and 1998, respectively. The implementation of the guidelines previously required human frame-by-frame review, but the U.K. guidelines have been implemented in an automatic screening device that is now widely used among U.K. broadcasters, developed by Cambridge Research Systems (140). The equipment analyzes a video sequence for flashes in relevant frequency ranges, flashing red, and certain visual patterns. Potentially provocative material is thereby identified and removed before transmission.

Broadcast screening clearly is desirable, but it does not prevent exposure to provocative sequences of images on video games. The games can be played interactively in countless pathways, so that the visual features may be different each time the game is played. However, sequences from games still can be assessed for risk, while recognizing that all possible play sequences cannot be examined.

Prevention of exposure

Computer-controlled video filters can be developed to attenuate the effect of flicker. These are called "adaptive temporal filters." Such a filter (141) was used to modify the notorious Pocket Monster 12-per-second 4-s segment of red flashing eyes. The original cartoon evoked a PPR in 11 susceptible patients. After processing by the adaptive temporal filter, the TV image no longer produced EEG changes in any of the patients. A recent study (142) claimed computer-mediated reduction of the red–blue dynamic range could reduce seizure risk, with a relatively small impact on appearance of the image.

Several investigators have recommended glasses or lens filters to take advantage of the observation that bright light, perhaps especially bright red light (which can be attenuated by blue glasses), is more likely to provoke PPISs (98,109,112,143). Polarized and cross-polarized glasses can reduce susceptibility to problems from some visual stimuli (144,145). A recent study (146), however, advocated a more sophisticated optical filter (special eyeglasses), combining even attenuation over most of the visible spectrum, with an additional attenuation of long-wavelength light. These filters reduced PPRs from video screens in 90–95% of cases.

MEDICATIONS

Most physicians prefer to avoid use of AEDs in photosensitive patients, if possible. The first line of therapy is avoidance of video games, or modification of exposure along the lines described earlier. Prevention with special screens, protective glasses, and warnings can be helpful (147). If conservative therapy fails, or if PPISs coexist with spontaneous seizures, then several seizure medications have been advocated. Harding and Jeavons (3) reviewed medications that had previously been tried [trimethadione, phenacemide, amobarbital, phenobarbital, nitrazepam, diazepam, sodium valproate (VPA), phenytoin (PHT), and ethosuximide]. Rimmer and colleagues (148) showed that a single dose of VPA or the GABA metabolism inhibitor, vigabatrin (VGB), could inhibit EEG photosensitive responses. Some authors believed that VPA was most efficacious (39). Harding et al. (149), in a comparative study of photosensitive patients either treated with VPA or not treated, demonstrated that the drug was 78% effective in significantly reducing the photosensitive range and abolished photosensitivity in 50% of treated patients. Moller and colleagues (150) studied β-carbolines, a drug active on the GABA inhibitory neurotransmitter system in six patients, but sample size was too small for a conclusion. VPA was recommended for children with idiopathic generalized epilepsy (68), but those with seizures only during video games perhaps do not require AEDs. Benzodiazepines, particularly clonazepam (151), also have been found to be effective. A young boy with Lennox–Gastaut syndrome and pattern-sensitive seizures was responsive to bromocriptine, 5 mg tid (152). This is based on the theory that photosensitivity relates to transient decrease

of dopamine in the cerebral cortex. Occasionally seizure medicines can aggravate photosensitive epilepsy, as was reported in a case of a child given PHT (153). A small study supports the use of levetiracetam (154).

GUIDELINES

Recommendations to reduce risk of PPISs can be directed at manufacturers, consumers, or regulatory agencies. A group of international experts in photoconvulsive and pattern-sensitive seizures met in London in September of 1993 under the auspices of the British Epilepsy Research Foundation to form a consensus statement based on currently available information (155). They concluded, "There is no reasonable doubt that epileptic seizures may be precipitated by playing interactive computerized 'video-games,' a term used to include not only those games using an interlaced video monitor but also small hand-held liquid crystal displays and arcade games. . . ." Contributing factors to a seizure included a photosensitive response to the physical characteristics of a display screen, a photosensitive response to the visual contents of the game independent of hardware, seizure precipitation by specific cognitive activities or movements; seizure precipitation by nonspecific emotional factors; lowering of a seizure threshold by fatigue or sleep deprivation; and coincidental occurrence of a spontaneous seizure while playing a video game. The relative importance of these factors is uncertain, but photosensitivity was considered to be paramount. Recommendations to the consumer included the following:

1. While playing a video game, the screen should be <12 inches or the patient should sit ≥ 4 times the diagonal screen diameter from the screen;
2. Play for >1 h per session should be avoided, and sleep should be maintained;
3. People with a history or family history of epilepsy or photosensitivity should have an EEG examination with photic stimulation before playing video games;
4. People shown to be photosensitive and their caregivers should be made aware of the potential risks of seizures from video games and provide supervision where appropriate.

In 1994, the U.K. Independent Television Commission drafted recommendations directed at the broadcast and TV industry. Recommendations were updated in 1999 and again in 2001. The guidance note recommends against flashing lights or regions of high luminance at three or more cycles per second, and against high-contrast bars, alternating in the range of 2–3 cycles per visual degree subtended. Based on the Pocket Monster incident, in which alternating colors seemed to be at least as important as alternating luminance, recommendations have been extended to avoidance of color changes at frequencies more than three per second. However, truly isoluminant colors were not thought to be provocative for seizures. After the Pocket Monster incident, TV Tokyo adopted a similar set of guidelines, as did the Japanese National Association of Commercial Broadcaster and NHK. Numbers of PPISs in Japan increased from 1996 through 1999 and then began to decrease, which was attributed to enactment of these guidelines (156).

The International Telecommunications Union (ITU), a group affiliated with the United Nations, has issued guidelines. Further discussion of consensus opinions can be found in the companion article to this work (1).

CONCLUSIONS

Photosensitivity is marked by an abnormal EEG response to visual stimuli, typically light flashes or light–dark striped patterns. All studies attempting to estimate the precise frequency of photosensitivity in the general population are limited by subject-selection bias. The studies that do exist suggest a prevalence (number outstanding) of photosensitivity in the range of 0.3–3%. Photosensitivity is higher in the young and female population. Most people with photosensitivity will never have a seizure. The prevalence of photoconvulsive seizures in the general population is $\sim$1 per 10,000, and 1 per 4,000 individuals between ages 5 and 24 years. Incidence (annual new onset) of PPISs is 1 per 91,000 in the overall population, but 1 per 17,500 in the age range from 7 to 19 years. In the well-studied Pokemon incident in Japan, only 24% of children having a seizure during the cartoon ever had a prior seizure. This implies that three of four photosensitive individuals are unaware of their photosensitivity. People known to have epilepsy have from a 2 to 14% chance of having seizures precipitated by light or pattern. About 2% of people with epilepsy can have a seizure provoked by TV. The annual incidence of video game seizures may be $\sim$1 per 83,000 [1.2 per 100,000 in Quirk (51)], but is higher among 7- to 19-year-olds.

Mechanisms of photosensitivity are only dimly understood. Animal models are available but may not closely approximate the human disorder. Normal occipital cortex comprises brain cells that respond to features of visual input: including light, edges, contrasts, orientation of edges, and motion light–dark interfaces across the retina. Because each cortex appears to have independent thresholds, the risk for a seizure induced by a visual stimulus is proportional to the area of visual cortex activated by a stimulus within a cerebral hemisphere, with unilateral hemisphere activation being almost as powerful an activation as is bilateral activation (80). Stimuli in the central visual fields (10% of the full fields) are more potent for

provoking seizures than are stimuli of the same size delivered to the visual periphery, although peripheral visual stimuli are just as provocative if cortical magnification is taken into account. Genetic factors clearly play a role in photosensitivity, but neither the role nor the genes involved have been identified.

Although light stimulation can trigger a seizure in photosensitive individuals, no evidence suggests that it can create epilepsy, a condition marked by spontaneously recurrent seizures. No data point to neuronal injury or loss from typical photic or pattern-induced seizures, although such damage might be speculated to exist in the rare cases of photoconvulsive status epilepticus.

Intensity is one of the two most important characteristics of light stimuli able to provoke seizures. Intensities of 0.2–1.5 million candlepower are in range to trigger PPISs. Frequency (flash rate) is the second key variable in provocation of a photic- or pattern-induced seizure. Frequencies in the range of 15–25 Hz are most provocative, but some individuals are sensitive to single flashes or to frequencies as high as 65 Hz. Light–dark borders can induce pattern-sensitive seizures, especially with a pattern oscillating in a direction perpendicular to the line of the pattern, having 2–3 spatial cycles per degree subtended at the eye. Only rarely will flashes or patterns occupying $<25\%$ of a TV or videogame screen provoke seizures. Patterns with bright stripes no brighter than 50 cd/m^2, or lasting for <0.5 s, also rarely induce seizures. Color is a controversial factor. Some believe that red colors or alternating red–blue oscillations can provoke seizures, but others think this unlikely if the brightness of the colors is matched. Rare patients self-induce PPISs by blinking, head-nodding, waving their fingers in front of their eyes, or intentionally looking at striped patterns.

TV-induced seizures result from combinations of sensitivity to flashing lights and patterns due to the TV-set flicker itself, and also to flash or patterns in the content of the program. Because of differences in line current frequencies in Europe versus the United States and Japan, TV flicker is more apparent in Europe and closer to the frequencies likely to provoke seizures. However, NTSC TV (the technical protocol used in the United States) does not provide protection against provocative program material. Certain video games also present flash and patterns of a type able to induce seizures in photosensitive players or observers. Identifying which factors are relevant for increasing risk is more difficult for videogames than for broadcast or recorded TV, because games can be played in so many different ways. Human factors, such as fatigue, excitement, sleep deprivation, and monocular versus binocular vision, may all play a role in PPISs, but especially in actively played games. Video games pose a minor risk for people with no known photosensitivity. Surveys suggest that the public, including patients with seizures not provoked by light, overestimate the risk for seizures provoked by video games.

Many authors have published recommendations about PPISs directed at patients, physicians, device or software manufacturers, and governmental agencies. No final set of recommendations yet exists, but European and Japanese groups have compiled extensive experience. International organizations, including the International Telecommunications Union (affiliated with the UN) and the International Standards Organization, are considering international guidelines. In the latter case, the guidelines would apply not only to TV broadcast and videogames, but also to a broad range of visual stimuli. The guidelines for industry in the United Kingdom and Japan emphasize the value of limiting bright flashes at frequencies higher than three per second. Light–dark stationary, oscillating, or reversing patterns should not have more than five stripes, unless they are restricted to $<25\%$ of the screen or are <50 cd/m^2 in brightness.

People with epilepsy or known photosensitivity have been advised to sit >2 m from a screen, to use good ambient lighting to reduce contrast, to avoid looking at rapidly flashing lights or alternating geometric patterns, to play video games for less than an hour at a time, to avoid sleep deprivation, and to cease play at onset of unusual visual symptoms, jerking, or blackouts. Closing one eye or looking away from the image is of more benefit than is closing both eyes.

The Photosensitivity Task Force of the Epilepsy Foundation of America believes that a seizure from visual stimulation represents a significant public health problem. No known method can eliminate all risk for a visually induced seizure in a highly susceptible person, but accumulation of knowledge about photosensitivity is now at a level sufficient to develop educational programs and procedures in the United States that substantially will reduce the risk for this type of seizure.

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