Review article with video sequences

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Photosensitivity: epidemiology, genetics, clinical manifestations, assessment, and management

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ABSTRACT – Photosensitivity is a genetically determined trait that may be asymptomatic throughout life or manifest with epileptic seizures. Photosensitivity usually begins before the age of 20 years with a peak age at onset at around 12. Both natural and artificial light may trigger seizures. Precise investigation must be carried out by intermittent photic stimulation that can elicit a clearly defined EEG response; video-EEG samples are reported to illustrate the various determinants of response and the main factors altering the effectiveness of intermittent photic stimulation. Management of photosensitive epilepsy includes non-pharmacological (*e.g.* avoidance of the provocative stimuli and wearing appropriate tinted glass) and pharmacological treatment. This review focuses on the emerging aspects of photosensitivity, in particular, the new guidelines for intermittent photic stimulation and briefly addresses epidemiological (in non-epileptic and epileptic subjects), genetic, diagnostic, and therapeutic issues. [*Published with video sequences*]

Key words: photosensitivity, photoparoxysmal response, epileptic, genetic, diagnosis, treatment

It has been known for more than a century that flickering sunlight can provoke epileptic seizures in susceptible patients (Gowers, 1885). Visual stimuli are the most common external factors triggering seizures in humans, and, therefore, photosensitive epilepsy (PSE) is the most common form of reflex epilepsy in humans (Naquet, 1987; Harding and Jeavons, 1994; De Bittencourt, 2004). Besides sunlight, seizures are also provoked by artificial light, striped patterns and, in the last decades, particularly by television and video games (Kasteleijn-Nolst Trenité *et al*., 2004). PSE came to greater public attention when about 700 children and adolescents were admitted to hospital because of seizures provoked by a Pokemon television cartoon (Takada *et al*., 1999; Takahashi *et al*., 1999a). Photosensitivity is defined as the presence of an abnormal response, called a "photoparoxysmal response" (PPR),

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to intermittent photic stimulation (IPS) during an electroencephalogram (EEG) (Covanis, 2005; Kasteleijn-Nolst Trenité, 2006; Verrotti *et al*., 2009). A PPR consists of irregular spikes or spikes-and-waves, ranging from a localised form of occipital spikes (Grade 1) to the most generalised form (Grade 4) of generalised spikes-and-waves or polyspike waves (Waltz *et al*., 1992; Lu *et al*., 2008) (*table 1*). Many different clinical situations are found in the context of photosensitivity and epilepsy. Patients may have seizures that are exclusively (or predominantly) visually induced, sometimes known as "pure photosensitive epilepsy" (Covanis *et al*., 2004). Alternatively, the patient may demonstrate photosensitivity as an EEG response to IPS in the laboratory and the epilepsy may be of any type, with or without visually induced seizures (Guerrini and Genton, 2004). Photosensitivity alone does not constitute an epileptic syndrome, as it can be present in all the main categories of epileptic disorders (Doose and Waltz, 1993; Appleton *et al*., 2000; Shiraishi *et al*., 2001).

Here, we review the current understanding of photosensitivity, PPR, and epileptic syndromes, and provide an update of epidemiology, genetics, assessment, clinical symptoms, and treatment.

Epidemiology

Incidence and prevalence of photosensitivity in the general population

PPRs are well documented in apparently normal subjects, especially children and adolescent girls (Driver and Mac Gillivray, 1976; Nagarajan *et al*., 2003). The highest rate of photosensitivity is most often detected around puberty, with a clear female preponderance (female:male; 2:1), perhaps due to hormonal influence (Wolf and Goosses, 1986; Kasteleijn-Nolst Trenité, 1989; Clement and Wallace, 1990; Familusi *et al*., 1998). However, video game-related seizures are more often found in males than females (Graf *et al*., 1994; Ferrie *et al*., 1994). Photosensitivity declines after the age of 15 years in around a third of patients (Harding *et al*., 1997; Anyanwu *et al*., 2003; Verrotti *et al*., 2004). In particular, some authors (Wolf and Goosses, 1986; Shiraishi *et al*., 2001) reported a high prevalence of PPR in the age group of 11-15 years with a decrease after 20 years of age. The prevalence of photosensitivity in non-epileptic subjects ranges from 0.5 to 8.9% of the population (Kooi *et al*., 1960; Quirk *et al*., 1995; Takahashi *et al*., 2001; Verrotti *et al*., 2002). The annual incidence of cases of visually sensitive epilepsy and PPRs was estimated to be 1.1 per 100,000 (Quirk *et al*., 1995). In the age range 7-19 years, the annual incidence rose to 5.7 per 100,000 (10% of all new cases) (De Bittencourt, 2004). Doose and Gerken (1973) found PPRs in 7.6% of 662 normal children with female preponderance (Jeavons *et al*., 1986). Binnie and Jeavons (1992) reported prolonged PPR in around 2% of non-epileptic people.

In male school children, Papatheophilou and Turland (1976) observed a PPR during standard IPS in 1.3% of normal school boys; a similar percentage was found in a study performed in Teofilo Otoni (Brazil) by Kasteleijn-Nolst Trenité *et al*. (2003).

Moreover, there are other large population studies on EEG photosensitivity in air force studies; a Danish Air Force study (Trojaborg, 1992) found a somewhat higher number of EEG abnormalities in 2.4% of 5,893 asymptomatic applicants. Among 13,658 men aged 17-25 years applying for Royal Air Force training, 48 (0.35%) demonstrated photoparoxysmal EEG responses (Gregory *et al*., 1993). Male candidates for aircrew training in the Netherlands and India showed PPR rates of 0.5 and 0.7%, respectively (Hendriksen and Elderson, 2001; Roy *et al*., 2003). The only reported population-based incidence study was performed after reports of seizures provoked by the Nintendo video game Mario World in 1992 (Quirk *et al*., 1995). The 16th December 1997 Pokemon incident in Japan provided an inadvertent "experiment-in-nature" to judge the prevalence of photic-induced seizures in a population of children; a nationwide retrospective study was undertaken to collect data on all patients with seizures within a two-month period after the broadcast. In a Pocket Monster cartoon, a rocket launch sequence with a flashing red then blue screen, changing 12.5 times per second for four seconds, resulted in hospital visits of 685 children (Harding, 1998; Ishida *et al*., 1998; Takahashi and Tsukahara, 1998). Subsequent studies suggested that

Table 1. The different patterns of photoparoxysmal response (Waltz *et al*., 1992; *Lu et al*., 2008).

Grade	Type of PPR
Grade 1	Spikes within the occipital rhythm
Grade 2	Parieto-occipital spikes with a biphasic slow wave
Grade 3	Parieto-occipital spikes with a biphasic slow wave and spread to the frontal region
Grade 4	Generalised spikes and waves or polyspikes and waves

≥560 of these children had seizures, although some had migraines, visual distortions, nausea and motion sickness, or other non-seizure symptoms (Takada *et al*., 1999), and more than half the children who had experienced a previous convulsion had a history of a seizure induced by television (Iinuma, 1998). Given that seven million children were watching the children's program, this suggests that roughly 1‰ of the Japanese population under the age of 18 had seizures after watching the cartoon (Furusho *et al*., 2002).

The prognosis associated with these EEG discharges in non-epileptic subjects is not fully established. Two studies have demonstrated that rarely the visual sensitivity detected in normal individuals evolves into epilepsy (So *et al*., 1993; Verrotti *et al*., 2002). So *et al*. (1993) reported an interesting evaluation of seizure-free patients who showed a PPR on IPS and found that the mere presence of a PPR is not a risk factor for developing seizures, because none of the 33 individuals showed seizures over the subsequent 6-12-year period. More recently, we studied 14 non-epileptic children who showed PPR without any other EEG abnormalities (Verrotti *et al*., 2002). During the whole period of follow-up of 7.1±1.1 years, no patient showed epileptic seizures, confirming that the presence of PPR should not be considered a marker for the development of epilepsy.

Incidence and prevalence of photosensitivity in patients with epilepsy

Clinical photosensitivity was found in 2% of patients of all ages with seizures and 10% of patients in the 7-19-year age range (Panayiotopoulos, 2005). Typical PPRs are associated with epilepsy in approximately 95% of the cases and occur in 5% of patients with epilepsy (Covanis, 2005).

Studies in epileptic patients show that an epileptiform response to IPS is found in about 10-20% of children and 5-10% adults, and the response is more common in females at any age (Kasteleijn-Nolst Trenité, 1989; Zifkin and Kasteleijn-Nolst Trenité, 2000). Some studies regarding the prevalence of a PPR have been carried out in cohorts of epileptic patients. Wolf and Goosses (1986) studied 103 patients of all ages showing a PPR on EEG; of patients with generalised epilepsies, 15% had photosensitivity, compared with only 3% in patients with localisation-related epilepsies. Among the various syndromes, the highest prevalence of PPR was found in juvenile myoclonic epilepsy (JME) (30%), followed by childhood absence epilepsy (CAE) (18%), and West and Lennox syndromes (17%). In juvenile absence epilepsy (JAE), only 8-13% showed a PPR. Recently, Shiraishi *et al*. (2001) studied a similar type of cohort and also applied the 1989 syndromic classification; among a total of 2,187 unselected patients from a Japanese epilepsy centre (age range 1-81; mean 24.2 years; 56% male), 37 patients (1.7%) were found to have a generalised PPR. Most PPR positive patients were found among idiopathic generalised epilepsy (IGE) patients (5.6%), compared to localisation-related epilepsy (0.7%). Within the IGE group, both JME (17.4%) and grand mal on awakening (7.6%) were significantly over-represented, while occipital lobe epilepsy (6.1%) was over-represented in the localisation-related epilepsy group. Of the patients with symptomatic generalised epilepsy, 2.0% had a PPR. Although the overall prevalence rate in Japan is lower, the distribution among the various syndromes appeared to be the same as in Europe; the highest prevalence of PPRs is found in generalised epilepsies and especially in patients with JME. In another Japanese study (Aso *et al*., 1994), in 17 children with visually induced seizures, three different syndromes were found; JME, severe myoclonic epilepsy in infancy (SMEI), and localisation-related epilepsies. These results underline that a PPR response can be found in symptomatic, cryptogenic, or localisation-related epilepsies, as confirmed by other authors (Tassinari *et al*., 1988; Brinciotti *et al*., 1994). Moreover, PPRs can be found in neurodegenerative diseases, such as Lafora and Unverricht Lundborg (Guerrini and Genton, 2004) and even in mesial temporal lobe epilepsy (Fiore *et al*., 2003). Recently, Stephani *et al*. (2004) performed a retrospective study in which they investigated photosensitivity in different epileptic syndromes of childhood and adolescence; 46% of patients with generalised epilepsies showed photosensitivity compared to 20% with focal epilepsies. Photosensitivity was more common in IGE (epilepsy with grand mal on awakening: 74%; JAE: 56%; JME: 50%; CAE: 44%) than in focal types (idiopathic partial-Rolandic epilepsy: 23%; symptomatic/cryptogenic epilepsy: 16%). Distribution of the photosensitivity rate among the different syndromes of IGE was different from the data reported by Wolf and Goosses (1986) and Waltz *et al*. (1990); in their study the epileptic syndrome with the highest rate of photosensitivity was JME (Waltz *et al*., 2000; Appleton *et al*., 2000), whereas in the study performed by Stephani *et al*., the highest rate of photosensitivity was found in epilepsy with grand mal on awakening. Epileptic events have been reported to be induced by watching movies since the 1900s and watching television since the 1950s (Livingston, 1952; Kerson and Kerson, 2006). Television epilepsy is known to be the most frequent type of photosensitive epilepsy (Quirk *et al*., 1995). For nearly 10% of patients, there is a family history of television epilepsy, suggesting a role of genetic factors (Doose and Gerken, 1973). Many reports describe television-induced and video game-induced seizures (William *et al*., 1994; Funatsuka *et al*., 2003). Recently, a follow-up survey from Iran was performed to investigate television-provoked epilepsy

in a group of children (Etemadifar *et al*., 2008); of 1,705 patients with epilepsy attending the clinics, 30 (1.76%) patients under 12 years were diagnosed with television epilepsy. Of these, 17 (56.7%) were females and 13 (43.3%) were males. The mean age at the onset of seizure was 9.9±2.1 years. Children had absence (3.3%), myoclonic (3.3%), and generalised tonic-clonic (93.3%) seizures (GTCS) in response to intermittent photic stimulations. These findings are in line with previous studies that have reported the most common types of seizures to be generalised tonic-clonic, followed by myoclonic and absence seizures (Covanis, 2005; Petrukhin *et al*., 1997). The strong association between television epilepsy and IGE has been reported in previous studies (Wolf and Goosses, 1986; Guerrini and Genton, 2004; Radhakrishnan *et al*., 2005).

Genetic aspects

There is a large amount of evidence for a genetic component of photosensitivity from both animal and human studies (Silva-Barrat *et al*., 1986; Neubauer *et al*., 2005; Grosso *et al*., 2006; De Kovel *et al*., 2010). Taken together, familial occurrence, association with IGE and monogenic disorders, evidence from genetic and experimental animal models, and the increased risk in siblings suggest a genetic component of photosensitivity. Evidence for a genetic component for the PPR endophenotype is provided by twin and family studies. Case reports of monozygotic twins show almost 100% concordance (Davidson and Watson, 1956; Herrlin, 1960); siblings of children with generalised PPRs are much more likely to show a similar abnormality than siblings of control subjects (19.3 *vs* 3.4%) (Doose and Gerken, 1973). In particular, Waltz and Stephani (2000) performed a study in families with a single photosensitive parent and showed that PPR is significantly more common in 5- to 10-year-old siblings of proband offspring of a parent with a PPR (50%) than in siblings of PPR-positive children of parents without a PPR (14%). This study and other systematic family studies have provided data for an autosomal dominant transmission with age-dependent penetrance of the PPR. Prevalence of PPR in relatives of PPR-positive subjects is independent of the underlying type of epilepsy (Davidson and Watson, 1956; Waltz *et al*., 1992; Waltz and Stephani, 2000; Stephani *et al*., 2004). In some families, PPR seems to segregate independently of the epilepsy phenotype, indicating that it is not a by-product of epilepsy (Doose and Gerken, 1973; Newmark and Kiffin Penry, 1979).

Gender may also influence PPR phenotype and certain studies have shown up to 2.5-fold higher prevalence of the PPR trait in girls (Harding and Jeavons, 1994); this may be caused by differences in hormonal levels, which may also be the cause of the distribution of age-related onset. Alternatively, the influence of gender could be related to the two X chromosomes (gynecotropism) by genetic or epigenetic mechanisms or due to direct or indirect protective effects of the male sex chromosome (Stephani *et al*., 2004; Taylor *et al*., 2007). Moreover, the incidence of epileptic seizures is elevated in female relatives of PPR carriers (when siblings of the mother and father are compared) (Doose *et al*., 1969).

It is, therefore, obvious that PPR is an epilepsy-related EEG trait with a high prevalence in idiopathic epilepsies (Covanis, 2005; Greenberg and Pal, 2007). In order to understand the molecular genetic basis of PPR, the variability of the associated epilepsy phenotypes must be taken into account. In some families, the association between PPR and epilepsy may be coincidental, resulting in comorbidity of the traits by chance, given the relatively high prevalence of PPR in the general population (Kasteleijn-Nolst Trenité *et al*., 2005). However, some observations suggest that there may be a causal relationship with the type of epilepsy. In particular, it is known that generalised PPRs (types III and IV) are mostly associated with IGEs (So *et al*., 1993; Fylan *et al*., 1999; Verrotti *et al*., 2002), such as JME (30-40%) and CAE (13-18%) (Wolf and Goosses, 1986). This high degree of comorbidity supports a role for PPRs in the predisposition of IGE. Moreover, it was also hypothesized that, depending on the stimulus, different types of pathophysiological mechanisms could elicit a PPR (wavelength-dependent or quantity-of-light-dependent PPRs) and that this would be related to the underlying epileptic syndrome (Takahashi *et al*., 1999b). It is possible that variation in more than a single gene can cause different PPRs, each associated with a certain epilepsy phenotype and respective syndrome-specific or seizure type-specific genetic factor. On the other hand, a single PPR gene could be modulated by different underlying epilepsy phenotypes to give rise to different PPR types (Kasteleijn-Nolst Trenité *et al*., 2005). Thus far, three molecular genetic studies on PPRs have identified putative loci on chromosomes 2, 6, 7, and 16. The loci seem to be correlated with a predominant seizure phenotype; evidence for linkage at 7q32 and 16p13 was found in PPR families with a prominent myoclonic epilepsy background (Pinto *et al*., 2005). These genomic regions contain genes that could be important for the neuromodulation of cortical dynamics in humans, such as the genes encoding the metabotropic glutamate receptor 8 (*GRM8*) and the cholinergic-muscarinic type 2 acetylcholine receptor M2 (*CHRM2*) (Parra *et al*., 2005); the genomic regions 6p21 and 13q31 were found in PPR families with a background of absences and partial epilepsies (Tauer *et al*., 2005). Chromosome involvement

was also suggested in a child with refractory myoclonic photosensitive epilepsy (Van Esch *et al*., 2002). Recently, suggestive linkage peaks were identified at 5q35.3, 8q21.13, and 16q13. Previous analyses had been performed in smaller sets of PPR families, which were collected by single laboratories; these analyses resulted in significant evidence for some loci that were no longer supported in the combined study.

Moreover, a study performed by Von Spiczak *et al*. (2010) investigated an association between PPR and sequence variations of the transient receptor potential cation 4 (*TRPC4*) gene. TRPC channels are involved in the generation of epileptiform discharges and *TRPC4* constitutes the main TRPC channel in the central nervous system. Thirty-five single nucleotide polymorphisms within *TRPC4* were genotyped in 273 PPR probands and 599 population controls. Association analyses were performed for the broad PPR endophenotype (PPR types I–IV; n=273), a narrow model of affectedness (PPR types III and IV; n=214), and PPR associated with IGE (PPR/IGE; n=106) for each SNP and for corresponding haplotypes. An association was identified between intron 5 SNP rs10507456 and PPR/IGE both for single markers (p=0.005) and haplotype level (p=0.01). Three additional SNPs (rs1535775, rs10161932, and rs7338118) within the same haplotype block were associated with PPR/IGE at p=0.05 (uncorrected) as well as two more markers (rs10507457, rs7329459) located in intron 3. Again, the corresponding haplotype also showed association with PPR/IGE, suggesting an association between *TRPC4* variants and PPR/IGE. Further studies including larger samples of photosensitive probands are required to clarify the relevance of *TRPC4* in PPR and IGE. Despite intensive research, the genetics of photosensitivity and of the relationship between photosensitivity and epilepsy are not yet completely understood (Guerrini and Genton, 2004; Stephani *et al*., 2004; Greenberg and Pal, 2007). Standardisation of methodology of photic stimulation as well as precise phenotyping seems crucial in further elucidating the genetic pathways.

Clinical aspects

Photosensitivity can be found in three different clinical conditions:

Epileptic syndromes in which IPS-induced seizures are absent. Many epileptic syndromes, regardless of aetiology of the epilepsy, can be associated with photosensitivity even though seizures induced by IPS never occur.

Epileptic syndromes in which both spontaneous and photo-induced seizures coexist. JME, generalised epilepsy with GTCS during wakefulness, Dravet syndrome, eyelid myoclonia with absences (EMA) (Striano *et al*., 2009; Capovilla *et al*., 2009) , progressive myoclonus epilepsy, and CAE.

Pure photosensitive epilepsies in which seizures are always and exclusively provoked by IPS. Background EEG activity is normal and in 60% of patients there are no EEG abnormalities, although photosensitivity is detectable. Traditionally, photo-induced seizures have been considered to be mostly generalised, however, video-EEG recordings have shown a clear preponderance of focal seizures and a minority of myoclonic seizures (Hennessy and Binnie, 2000), and the true existence of GTCS induced by IPS is still a matter of debate. A recently-described variant of benign myoclonic epilepsy (Capovilla *et al*., 2007) in which myoclonic manifestations are exclusively related to IPS should be included in this group.

Purpose and assessment of photosensitivity

The purpose of intermittent photic stimulation

Photosensitivity may be observed as an occasional finding during an EEG recording or specifically identified during both diagnosis and therapy. IPS can be useful to either confirm the diagnosis of the epileptic nature of an episode that occurred during photostimulation or evaluate subjective feelings related to photostimulation. Moreover, IPS can help the physician to evaluate the usefulness of protective lenses, evaluate the efficacy of an antiepileptic therapy, and counsel patients.

Assessment of intermittent photic stimulation

The assessment of photosensitivity requires a precise methodology (Kasteleijn-Nolst Trenité *et al*., 1999; Rubboli *et al*., 2004; Kasteleijn-Nolst Trenité *et al*., 2012). The goal is to obtain a clear description of standardised methods, applicable to every EEG laboratory. IPS should be performed before or at least three minutes after hyperventilation in a dim room, so that the patient may be visible.

The stroboscopic light (a round lamp which flashes with an intensity of at least 0.7 Joules) should be positioned at a distance of 30 cm from the nasion (*video 1*). The patient should be instructed to look at the centre of the lamp and close eyes when necessary. If this is not possible, someone else should close the eyes and keep them closed. During the first 5 seconds, the patient should have eyes open and then closed for another 5 seconds. This sequence offers the possibility to study three different conditions: eyes open, eye closure, and eyes closed. Alternatively, the eye closure condition may be chosen with stimulation using a frequency of 7 seconds per flash. The interval between

stimulations should be almost 7 seconds and frequencies explored between 1 and 60 Hz. The photosensitive range should be determined as precisely as possible. IPS should be stopped immediately after the onset of generalised discharge on EEG. Video-EEG recording, polygraphy, and questioning patients are necessary in order to identify even the most subtle clinical manifestations related to IPS. In the case of generalised EEG discharges, patients should be tested both with arms at rest and arms in the Mingazzini I position (*video 2*) to detect possible positive or negative myoclonic manifestations by video and polygraphy. The use of two video cameras offers the possibility to simultaneously detect the body and the face of the patients.
In the case of seizures induced by television and video games, visual pattern can be tested during EEG to confirm a possible effect of the video game. Factors that influence photosensitivity are related to stimulus: frequency, duration, stroboscopic power, open or closed eyes, eye closure, and interval between different stimulations. Other factors are related to the patient (sleep deprivation, circadian rhythm, and menstruation), as described by some authors (*video 3*), or are totally independent, such as room luminance, mono or binocular vision, and locus of foveal stimulation (*videos 4 and* 5).

Treatment

The aim of treatment is to prevent reflex seizures and avoid nociceptive stimuli.
Patients with photosensitivity often describe an unpleasant subjective feeling related to IPS and have a particularly anxious feeling prior to an imminent seizure. Treatment can be based on either antiepileptic drugs (AEDs) (keeping in mind possible inefficacy, adverse effects, and cost) or non-pharmacological measures to avoid or reduce provocative stimuli.

Pharmacological treatment

Pharmacological treatment should be based on AEDs which are effective for the specific type of epilepsy of the patient (Verrotti *et al*., 2005). There are many reports of treatment for photosensitivity and many AEDs have been evaluated; lamotrigine (Binnie *et al*., 1986; Richens and Yuen, 1991), vigabatrin (Rimmer *et al*., 1987), levetiracetam (Kasteleijn-Nolst Trenité *et al*., 1996; Striano *et al*., 2007), valproate (Patry and Naquet, 1971; Bruni *et al*., 1980), and carisbamate (Trenité *et al*., 2007). Only one controlled trial is documented which examined the effect of sodium valproate (Harding *et al*., 1978), with efficacy in 61% of cases (*table 2*).

Table 2. Main studies on the pharmacological treatment of photosensitivity.

Antiepileptic drugs	Reference	Patients studied	Prognosis
Carisbamate	Trenité *et al*., 2007	18 patients	Dose-dependent reduction in photosensitivity in 13 patients in response to carisbamate.
Lamotrigine	Binnie *et al*., 1986	72 patients	Suppression of photosensitivity following a single acute administration of all the major AED groups.
	Richens and Yuen, 1991	Patients with frequent interictal spikes and refractory seizures	Efficacy for partial and tonic-clonic seizures; 30% reduction in partial seizures.
Levetiracetam	Kasteleijn-Nolst Trenité *et al*., 1996	12 patients	Clear suppression (3 patients) or abolishment (6 patients) of IPS in 9 of 12 (75%) photosensitive patients.
	Striano *et al*., 2007	28 patients	Responder rates were 64.2% for tonic-clonic, 60% for myoclonic, 60% for focal, and 44.4% for absence seizures.
Valproate	Harding *et al*., 1978	70 patients	In 27 patients, photosensitivity was abolished; in 12 patients photosensitivity was reduced.
	Bruni *et al*., 1980	22 patients	>75% improvement in 80% of patients with absence seizures, 40% with tonic-clonic seizures, all with myoclonic seizures, and 43% with partial seizures.
Vigabatrin	Rimmer *et al*., 1987	6 patients	Vigabatrin was compared with sodium valproate. Both drugs suppressed the photoconvulsive response in 3 of 6 subjects

Non-pharmacological treatment

In an attempt to prevent seizures, it is important to consider that some situations aimed at avoiding stimuli may often evoke photosensitivity. Both natural and artificial lights should be taken into account. In everyday life, it is impossible to avoid all photic stimulation; consequently, it is crucial to implement preventative measures with regards to the stimuli and patient. The risk of seizures induced by a television screen can be reduced by 100-Hz or LCD monitors. When watching television, the room should always be well lit and the distance from the patient to the monitor should be as much as seven times that of the monitor diameter. In some countries (Japan and the United Kingdom) there are broadcasting guidelines for the production of television material. The computer screen should be used at maximum refresh rate. Patients should be instructed to close only one eye when facing a potential stimulus and the effect of closing a particular eye may be tested during EEG ambulatory (Patient 1; *video 6 and figures 1, 2, 3, 4, 5, 6 and 7*). It is advisable to avoid other risk factors when possible (stress, sleep deprivation, and menstruation). Patients can also use a new type of lens for this purpose (after a long phase of testing and validation), investigated by two of the authors (GC and FB). Previous observations had demonstrated efficacy of blue lenses in controlling photosensitivity (Takahashi and Tsukahara, 1976; Takahashi and Tsukahara, 1992). Besides colour, we have also considered a dark shade of lens material and a first group of 20 photosensitive patients were tested (Capovilla and Dalla Bernardina, 1994). A particular kind of lens (named Z1), with a reduction of luminance of more than 80%, was very effective in controlling PPR in photosensitive epileptic patients. Thus, we tested the lens in a group of 83 patients, and compared it with four other types of available lenses (Capovilla *et al*., 1999) (*video 7*). Z1 lenses were demonstrated to be superior. In fact, PPR was suppressed in 77% of patients and reduced in 19%. A multicentre study tested 610 patients and Z1 efficacy was confirmed, irrespective of age, sex, AEDs, and epileptic syndrome (Capovilla *et al*., 2006). The lenses are now commercially available and can be graduated; therefore, for pure photosensitive epilepsies, AEDs may be avoided in order to prevent photo-induced seizures. For patients with spontaneous and photo-induced seizures, prescription of AEDs should be individually evaluated and photo protection is always recommended. For photosensitive subjects without epileptic seizures, AEDs are not recommended, but photo protection should be advised and the use of lenses encouraged, in particular, if an unpleasant subjective feeling is reported by the subject. □

Disclosures.
None of the authors has any conflict of interest or financial support to disclose in connection with the published text.

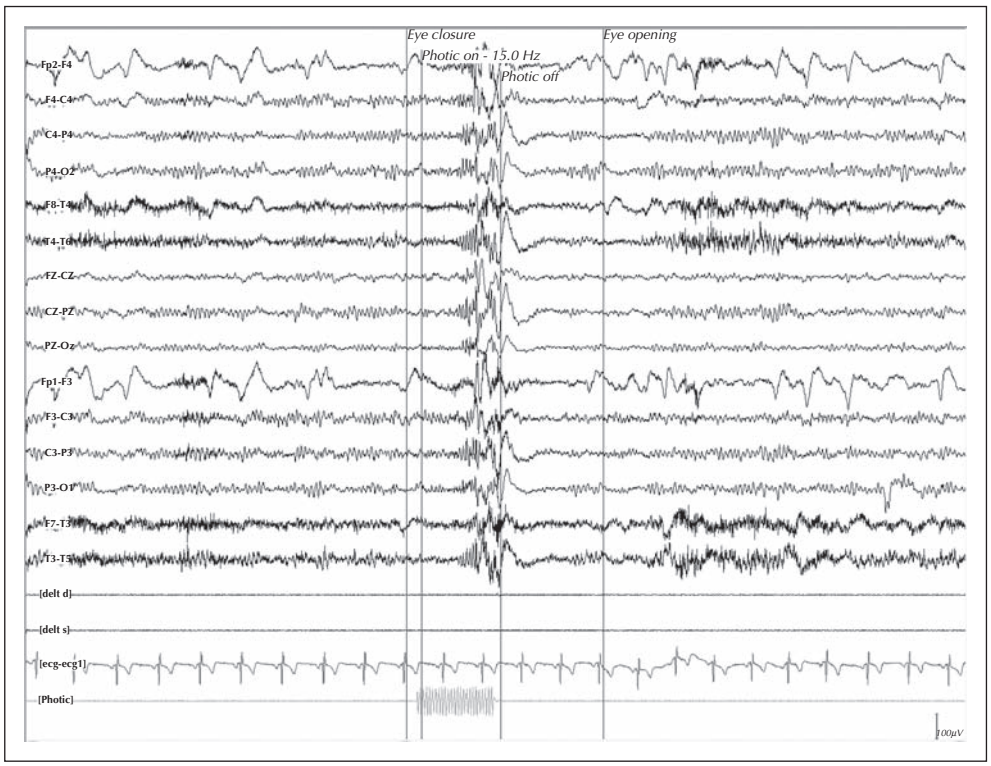

Figure 1. Intermittent photic stimulation performed at a frequency of 15 Hz induces photoparoxysmal response.

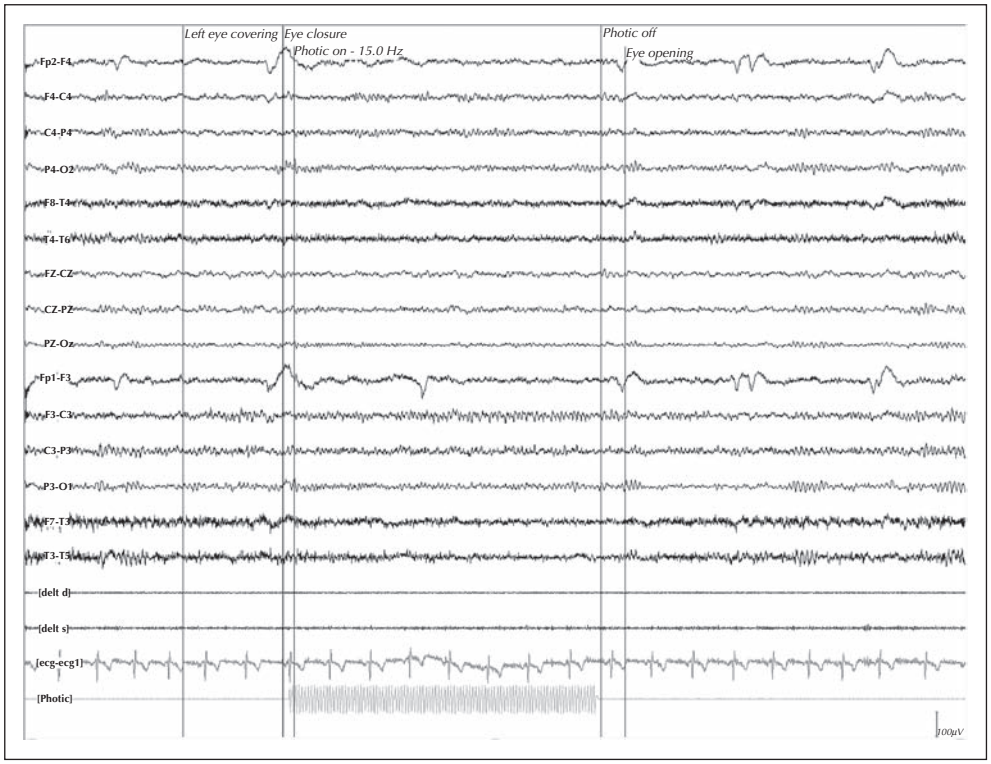

Figure 2. Covering of the left eye is effective in photoparoxysmal response control.

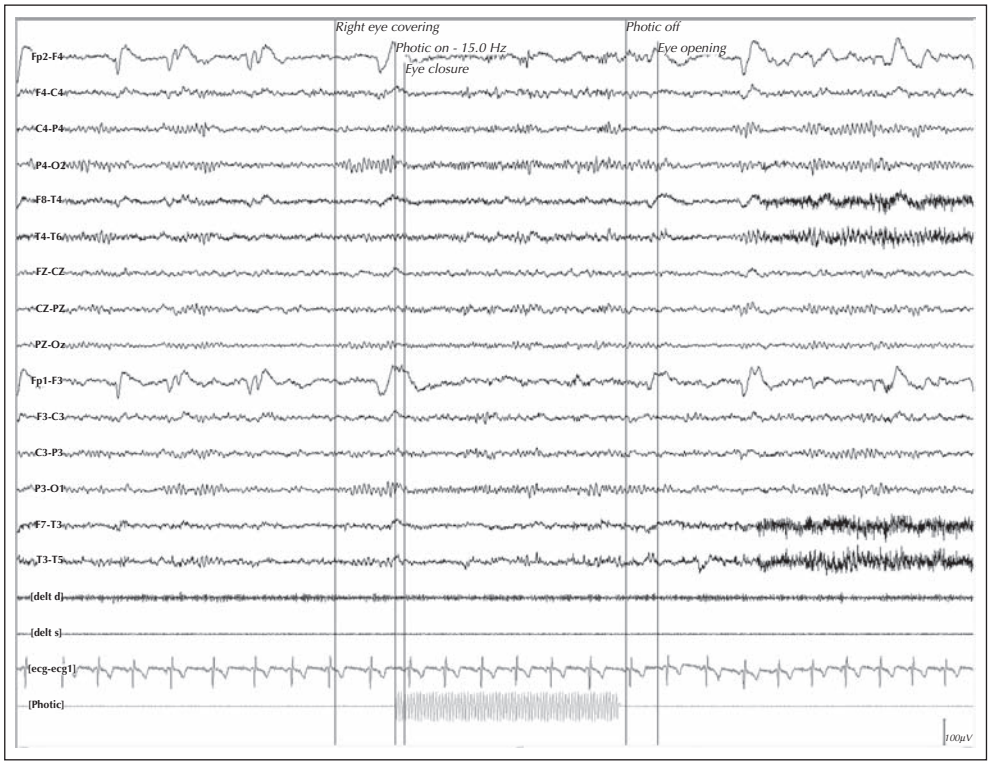

Figure 3. Covering of the right eye is effective in photoparoxysmal response control.

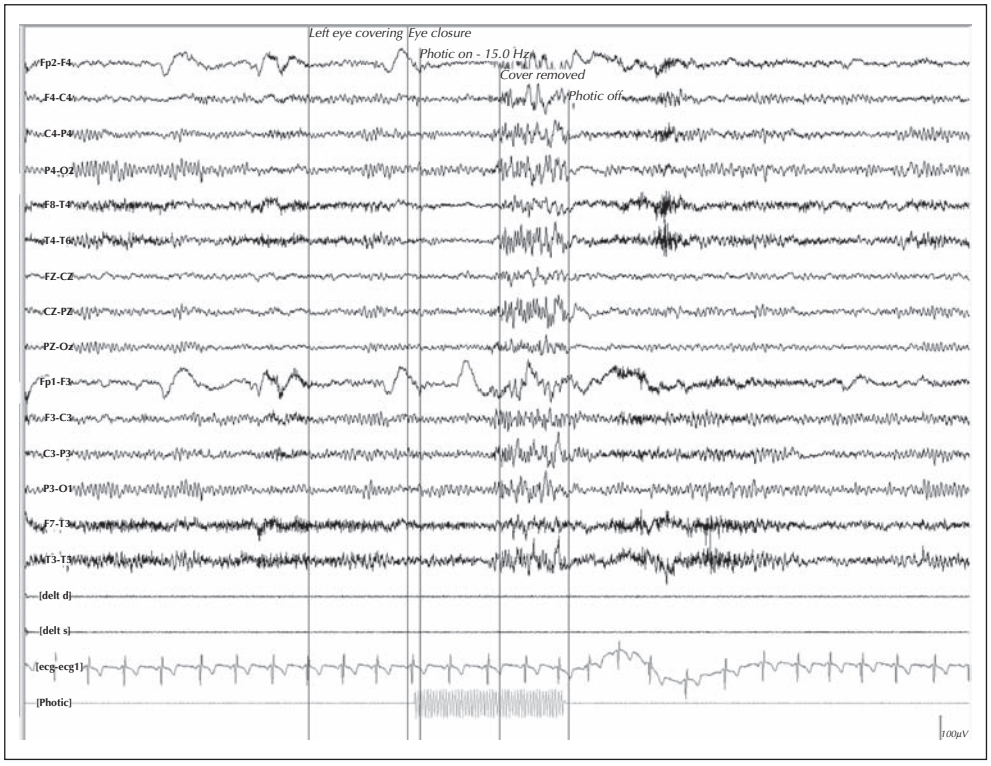

Figure 4. When the left eye is uncovered, photoparoxysmal response immediately reappears.

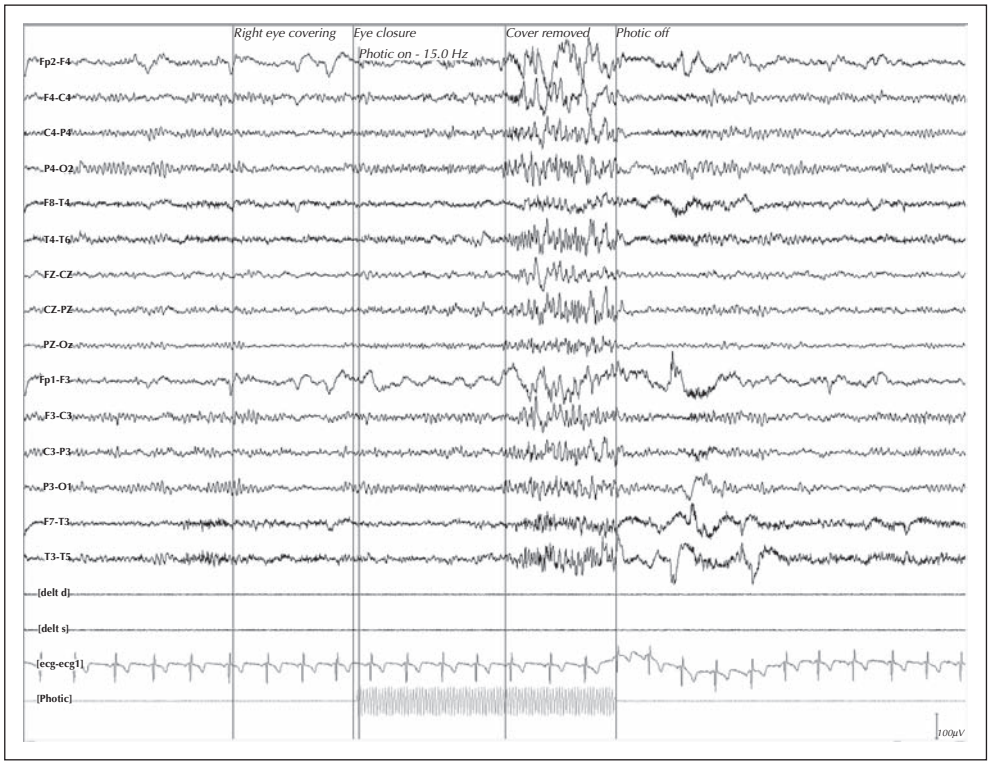

Figure 5. When the right eye is uncovered, photoparoxysmal response immediately reappears.

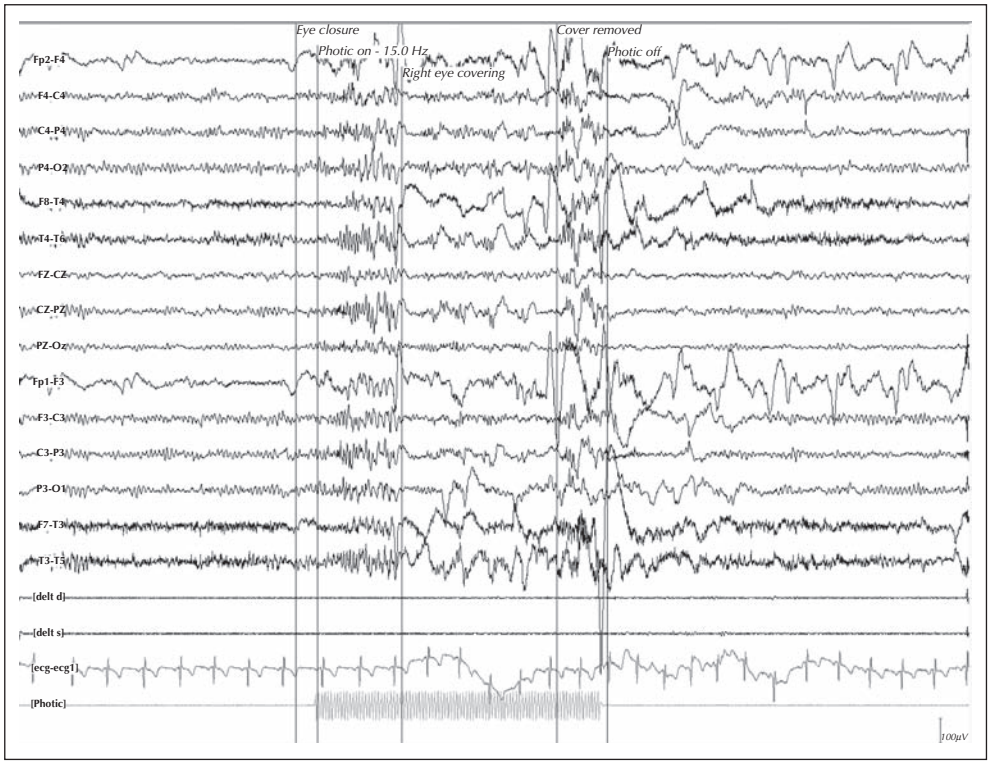

Figure 6. Covering of the right eye is also effective during photoparoxysmal response. Photoparoxysmal response immediately reappears if the right eye is uncovered.

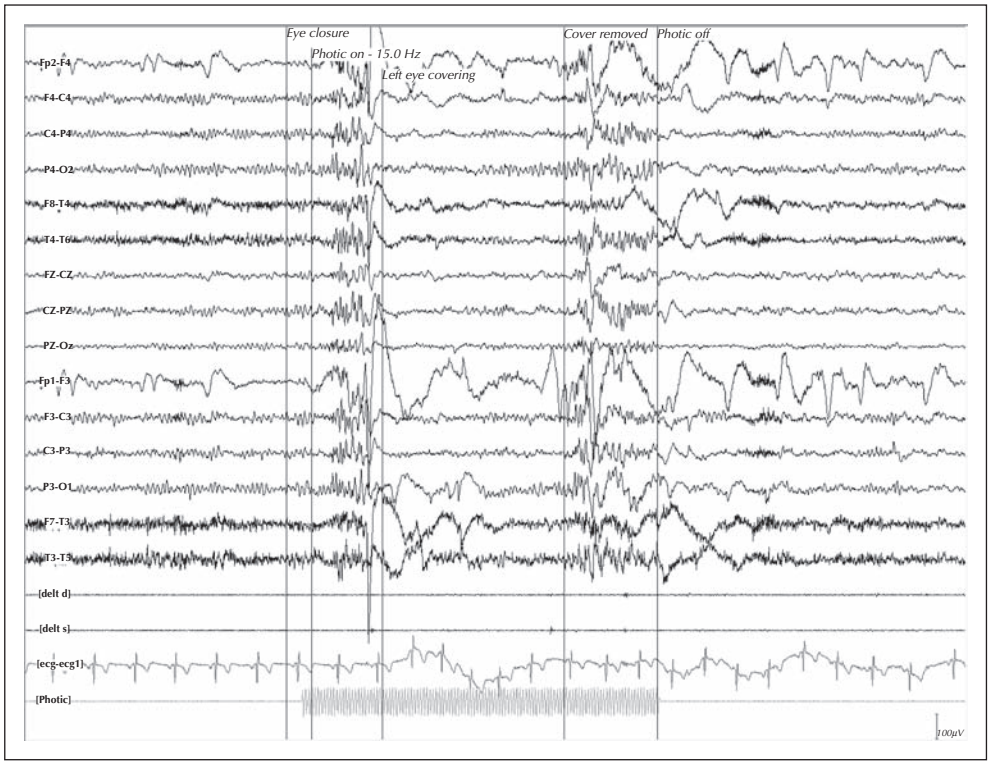

Figure 7. Covering of the left eye is also effective during photoparoxysmal response. Photoparoxysmal response immediately reappears if the left eye is uncovered.

Legends for video sequences

Video sequence 1

The lamp for IPS is positioned at a distance of 30 cm from the nasion. The room is in darkness to demonstrate the correct distance.

Video sequence 2

IPS is performed when the patient is holding his arms in the Mingazzini I position. Note the myoclonic-atonic phenomenon responsible for dropping the object which was in his hand.

Video sequence 3

A positive IPS response was obtained in an adolescent girl with JME soon after awakening (note the time of recording). IPS was ineffective when performed during afternoon EEG.

Video sequence 4

A five-year-old girl presents with typical absence seizures during IPS, but, unlike those of video 5, only when IPS is performed in a light room.

Video sequence 5

A young girl presents with typical absence seizures with mild clonic manifestations during IPS. If IPS is performed in a light room, as shown in the video, absence does not occur.

Video sequence 6

The video sequence shows that right eye closure is effective in PPR control, whereas left eye closure is relatively ineffective. This is evident if eye closure is performed at the start or during IPS.

Video sequence 7

Five different types of lenses are tested in a young girl with Janz Syndrome, comparing a special lens (Z1) with four (three blue and one brown) different commercial lens types. The first IPS is performed without a lens, the second, third and fourth with blue lenses, the fifth with a brown lens, and the sixth with a Z1 lens. Complete effectiveness is shown only with a Z1 lens. The first and sixth IPSs have the same frequency.

Key words for video research on www.epilepticdisorders.com
Syndrome: photosensitive epilepsy
Etiology: not applicable
Phenomenology: photosensitive
Localization: not applicable

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