

Adult-onset photosensitivity: clinical significance and epilepsy syndromes including idiopathic (possibly genetic) photosensitive occipital epilepsy

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ABSTRACT – To evaluate the clinical associations of adult-onset photosensitivity, we studied the clinical and EEG data of patients who were referred due to a possible first seizure and who had a photoparoxysmal response on their EEG. Patients with clinical evidence of photosensitivity before the age of 20 were excluded. Of a total of 30 patients, four had acute symptomatic seizures, two had vasovagal syncope, and 24 were diagnosed with epilepsy. Nine of the 24 patients had idiopathic (genetic) generalized epilepsies and predominantly generalized photoparoxysmal response, but also rare photically-induced seizures, while 15 had exclusively, or almost exclusively, reflex photically-induced occipital seizures with frequent secondary generalization and posterior photoparoxysmal response. Other important differences included a significantly older age at seizure onset and paucity of spontaneous interictal epileptic discharges in patients with photically-induced occipital seizures; only a quarter of these had occasional occipital spikes, in contrast to the idiopathic (genetic) generalized epilepsy patients with typically generalized epileptic discharges. On the other hand, both groups shared a positive family history of epilepsy, common seizure threshold modulators (such as tiredness and sleep deprivation), normal neurological examination and MRI, a generally benign course, and good response to valproic acid. We demonstrated that photosensitivity can first occur in adult life and manifest, either as idiopathic (possibly genetic) photosensitive occipital epilepsy with secondary generalization or as an EEG, and less often, a clinical/EEG feature of idiopathic (genetic) generalized epilepsies. Identification of idiopathic photosensitive occipital epilepsy fills a diagnostic gap in adult first-seizure epileptology and is clinically important because of its good response to antiepileptic drug treatment and fair prognosis.

Key words: EEG, photic stimulation, posterior photoparoxysmal response, occipital seizures, generalized epilepsies

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EEG photosensitivity is defined by the occurrence of the photoparoxysmal response (PPR) to intermittent photic stimulation (IPS). People with PPR on the EEG may already have (or later develop) a distinctive epilepsy syndrome with or without photically-induced seizures, have exclusively or almost exclusively photically-induced seizures (pure photosensitive epilepsy), or may not have or develop seizures at all. Focal seizures appear to comprise around 2.5% of the total photically-induced seizures across ages (Jeavons and Harding, 1975), although the percentage appears to be higher in children (Aso et al., 1988; Ricci and Vigeveno, 1993; Takada et al., 1999), rising up to 17% (Guerrini et al., 1998). A distinctive subgroup of children and adolescents with exclusive, or almost exclusive, photically-induced occipital seizures, positive family history, and normal neurological development and brain MRI has been described as *idiopathic photosensitive occipital lobe epilepsy* (Guerrini et al., 1995; Guerrini et al., 1997; Yalçın et al., 2000; Politi-Elishkevich et al., 2014).

Most photosensitive patients initially have photically-induced seizures or become only EEG-sensitive to lights during their childhood or adolescence (Jeavons and Harding, 1975; De Bittencourt, 2004; Panayiotopoulos, 2007) and about two thirds of them remain photosensitive as adults (Harding et al., 1997). Nevertheless, photosensitivity can be identified for the first time in adulthood (Scott and Elian, 1981), but little is known about its clinical significance and EEG/clinical presentation. Most, if not all, of the available relevant information comes from the earlier literature. Jeavons and Harding (1975) reported that 53 of their 454 patients were 20 years or older when they showed PPR on the EEG, but did not specify how many of these patients had already started having seizures before the age of 20 (whether they had spontaneous or photically-induced seizures, or both) or the types of photically-induced seizure they might have had. Newmark and Penry (1979) reviewed 35 earlier reports (from 1936 to 1976) and found 42 patients (17 males and 25 females) with EEG photosensitivity after the age of 20 years. The age at onset of photically-induced seizures was known in only seven patients (two males and five females), and these patients were all older than 20 years, however, the seizure type was described in only a few. Among the best described cases is that of a woman with two long photically-induced occipital seizures during two EEG recordings on consecutive days, at the age of 35 (Fischer-Williams et al., 1964). Seizures started from either side of the brain and were associated with formed visual hallucinations, autonomic symptoms, perioral automatisms, and aphasia (in the left-sided seizure), before they became secondary generalized. Her medical history was remarkable for “neurotic symptoms” and migraine, and there was no reference

of any epileptic seizures or photosensitivity before the age of 35, or alcohol intake. She had a second seizure two years later “while she was being driven in a car down a tree-lined avenue on a bright, sunny winter’s day”, but no further seizures over the four following years. In their retrospective EEG study, Scott and Elian (1981) reported 32 patients above the age of 30 years with “a seizure disorder” and PPR that was posterior in 14 and generalized in 18. None had a personal or family history of “petit mal”. Yet it is uncertain whether, and in how many of these 32 patients, environmental photic stimuli had provoked seizures and what their seizure type(s) might have been.

Prompted by suggestive earlier clinical and EEG observations (Sharief et al. [2000]; see also Panayiotopoulos, 2005, Panayiotopoulos [2005, 2010]) and the paucity of relevant information, we investigated the occurrence of photosensitivity in adult life, aiming to define:

- the conditions to which it can be related, including its association with adult-onset epilepsies;
- its clinical significance.

Patients and methods

We studied the clinical and EEG characteristics of patients with a first EEG with PPR above the age of 20; patients were recruited from our dedicated first-seizure clinic, prospectively since 2008, and from our tertiary epilepsy clinic. All patients referred with a possible first seizure were investigated by video-EEG (after partial sleep deprivation when possible) (Leach et al., 2006) and brain MRI. Patients with diagnosed epilepsies had follow-up EEG and imaging studies, as clinically required.

Our clinical and EEG methodologies for the diagnosis of epilepsies have been detailed elsewhere (Koutroumanidis et al., 2008), including our sleep-deprived EEG (SDEEG) recording protocol and interpretation (Bonakis and Koutroumanidis, 2009). Over the years of this study, digital video-EEGs have been recorded using a Nicolet Voyageur system (Nicolet Biomedical Inc, Madison, WI, USA) until 2004, a Nihon-Kohden Neurofax EEG-1100 system (Nihon Kohden Corporation, Tokyo, Japan) until 2012, and an XLTEK Natus system, according to the international 10-20 system. IPS was performed (after awakening on SDEEG) a few minutes after the last session of hyperventilation with the room dimly lit, according to the 1999 Consensus Proposal (Kasteleijn-Nolst Trenité et al., 1999). Patients were instructed to look at the centre of the strobe lamp, placed 30 cm from their eyes, and to report any symptoms they may experience during IPS. Uninterrupted trains of stimuli of about 10-12 seconds were given for each frequency, starting with the eyes open for around four seconds, during eye closure,

and finally with eyes closed for around four seconds. An ascending step-by-step sequence was performed at strobe frequencies of 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 25, 30, 40, 50 and 60 Hz, followed by a descending sequence in the reverse order when PPR occurred, to define the range of photosensitivity. Frequencies above 20 Hz were, on occasions, further elaborated to define the range more accurately. When a posterior PPR was elicited, the ascending sequence continued until a generalized PPR occurred; then the descending sequence was performed, again until a generalized PPR. Therefore, we attempted to obtain ranges for both posterior and generalized PPR when they co-existed. Stimulation at any frequency that elicited any PPR was repeated at least once (after an interval of 10-20 seconds) to confirm consistency, and the patient was asked about possible symptoms that were recorded by the physiologist; these were then compared with the EEG changes and the video footage.

We chose to describe the type of PPR in reference to the type of EEG used (routine vs. SDEEG) because sleep deprivation or post-awakening may enhance a change in posterior to generalized PPR, or reveal a posterior PPR that may be absent in routine recordings, as in Patient 4 (*table 1 and supplementary data*). In view of such dynamic variability, we distinguished only two types of PPR: *posterior stimulus-independent* when they were limited to occipital areas or spread to parietal, temporal or central areas; and *generalized* when they involved all leads, with or without posterior lead-in, and irrespective of whether they retained a posterior to anterior gradient or became maximal over the frontal areas.

Clinical photosensitivity and definition of the age at onset

We diagnosed *clinical* photosensitivity on the basis of:

- historical evidence that the “first” epileptic seizure that prompted the first EEG with PPR was highly likely to be associated with environmental light;
- reported symptoms or clinical signs associated with the PPR on EEG.

To define more precisely the onset of their clinical photosensitivity, all patients who fulfilled the above diagnostic criteria were interviewed in more detail, focusing on possible earlier photically-induced minor symptoms similar to the initial symptoms of their first major seizure, or to those elicited by IPS during the EEG. By the time of their referral, most of these adults had already used a PC, watched TV, or experienced strobe lighting in a night club, and were able to trace back similar symptoms, when these existed; those with clinical evidence of photically-induced symptoms before the age of 20 were excluded.

Despite such scrutiny, we cannot rule out that an earlier inconspicuous onset was not overlooked by some of our patients; for instance, it is known that some photosensitive patients may ignore IPS-induced mild unilateral twitches, or a fleeting cephalic, epigastric or visual sensation (Kasteleijn-Nolst Trenité et al., 1987), suggesting that similar symptoms induced by environmental light might have passed unnoticed. Nevertheless, with regards to the onset of clinical photosensitivity, it is pragmatic to consider the earlier age when symptoms *known* to be triggered by light can be identified by the patients.

The onset of EEG photosensitivity was possible to approximate only in the patients with previously diagnosed epilepsies and earlier EEGs with normal responses to IPS (Group 3).

Results

Since 2000, 34 adults (30 referred due to a possible first seizure and four of whom had already been diagnosed with epilepsy and followed in our epilepsy clinic) had a first EEG with PPR in response to IPS, without clinical evidence of any seizure symptoms associated with environmental sources of light, *before* the age of 20 years. Clinical follow-up ranged from 1 to 21 years (mean: 6 years), including the four patients who had been diagnosed with epilepsy without photosensitivity before 2000. Of the 30 patients with a possible first seizure, three each had a single acute symptomatic seizure (post-head injury with ensuing psychogenic seizures recorded on video-EEG in two and cerebral hypoxia due to severe type 2 respiratory failure in the third) that was not related to environmental light stimuli, two were diagnosed with neurally mediated syncope, and one had three alcohol withdrawal seizures. Syndrome classification was possible in nine of the remaining 24 patients with adult-onset epilepsies and in the four already diagnosed patients, referred hitherto as Groups 2 and 3, respectively. Group 1 included 15 patients with adult-onset epilepsy and photosensitivity, who were impossible to classify into formally recognized epilepsy syndromes (*tables 1 and 2*); five of those were amongst 240 consecutive patients with adult-onset epilepsies who attended the first-seizure clinic over the last five years (2%). This study mainly focuses on Group 1.

Group 1: Patients with photically-induced focal seizures

Family history/antecedents

The father of Patient 12 had a few seizures as an adult, while the father of Patient 11 had been diagnosed with photosensitivity as a teenager.

Table 1. Clinical data, including treatment and outcome.

Patient/Sex/ Age	Age at onset (years)	Age at first evaluation	Seizure symptoms / signs	Total/provoked* seizures/active phase	AED	Clinical outcome
1/M/33	31	31	Severe blurring of vision->GTCS	1/1/-	-	SF for 2 years; lost to f-u
2/M/35	22	30	Visual illusion of everything slowing down->being spun around twice->GTCS	3/2/8 years	VPA**	SF for 5 years; discharged on VPA
3/F/61	47	47	Feeling of right eye flicker, vision distortion/blurring-> "unable to form words although I knew what I wanted to say for few min" ->GTCS	5/4/10 years	-	SF for 4 years
4/F/52	33	48	Feeling of "internal shaking and unsteadiness and influx of intense light" followed by several minutes of amnesia; no convulsions	3/3/15 years	VPA	SF for 4 years; discharged off VPA
5/M/46	41	41	Visual distortion/blurring->GTCS	1/1/-	VPA	SF for 5 years
6/M/27	24	25	Oscillating diagonal lines->GTCS	2/2/ one year	VPA	SF for 3 years
7/F/34	31	33	Vision "jumbled/swirly" then blurred, left arm twitched, head pulled to left, disorientation; 2 CPS but no GTCS	<10/all/2 years	-***	SF for <1 year (avoiding night clubs and sleep deprivation); lost to f-u
8/M/44	41	41	"Lost focus"->GTCS	1/1/-	-	SF for 3 years
9/M/28	26	26	Cephalic/headache/dizziness/ disorientation/slurred speech (1 secondary GTCS)	4/3/3 years	-	SF for <1 year; lost to f-u
10/F/55	47	48	"Flashes in the movie, many small TV screens covering the entire visual field"; GTCS lasting a few sec.	>10/all/2 years	VPA	SF for 5 years; discharged off VPA
11/F/27	24	24	"Overwhelming sensation"; "dislike" to any source of light when tired (PC, TV, striped lighting), a few months after starting post-doc; 1-sec GTCS.	<10/all/2 years	-***	Symptoms have been reduced (reduced time on PC)
12/F/42	36	36	Version anti-clockwise, as though trying to pick things from just above her height -> GTCS	2/2/one year	VPA/LEV	SF for 6 years
13/M/44	35	35	Felt rough and odd at the back of his head for a while; strain in his eyes; disorientated	2/1/8 years	-	SF for 1 year
14/M/40	33	38	"strobe-like effect", multiple "jumping images" unable to focus, unwell for few minutes->GTCS	2/2/5 years	LTC****	SF for 2 years
15/M/35	32	32	Visual illusion of everything going much faster than himself	2/1/1 year	-	SF for 2 years

SF: seizure-free; f-u: follow-up; VPA: valproate; LEV: levetiracetam; LTC: lamotrigine; *on historical evidence; **the dose of VPA was 200 mg bd or 300 mg bd in all except in Patient 12 who was on 500 mg bd; ***Patients 7 and 11 declined treatment; ****the dose of LTC was 50 mg bd

Table 2. EEG findings including PPR and its persistence.

Patient/ Sex/ Age	Age at first EEG / Type	Interictal EEG abnormalities	First EEG (PPR / range)	Reported PPR-asso- ciated symptoms	Age at last EEG / type / AED	PPR response	Estimated* persistence of PPR
1/M/33	31 / R	-	Occipital- parietal / 14-20 Hz	-	-		Unknown
2/M/35	30 / R	-	Occipital- parietal / 18-20 Hz	-	35 / R / VPA	No	< 13 years
3/F/61	47 / R	-	Occipital to temporal (L>R), including eyes open / 14-30 Hz	Felt jerks	61 / R / no AED	No	< 14 years
4/F/52	48 / SD	-	Posterior to central-frontal / 12-30 Hz	Myoclonic jerks	50 / R / VPA 52 / SD / VPA	No Declining	> 19 years
5/M/46	41 / SD	OS on eye closure after awakening	Occipital to temporal / 14-16 Hz	-	44** / R / no AED	Declining	> 3 years
6/M/27	25 / SD	-	Occipital to central / 8-18 Hz	Squint and strain in eyes	-		Unknown
7/F/34	33 / SD	OS on eye closure after IPS	Occipital between 12-18 Hz; to temporal- central at 20 Hz	"Jumbled - swirly" vision	-		Unknown
8/M/44	41 / R	-	Occipital to central, including eyes open / 14-30 Hz	Out of body experience	-		Unknown
9/M/28	26 / R	-	Occipital / 20-25 Hz	Cephalic sensation	-		Unknown
10/F/55	48 / R	-	Occipital - parietal / 14-18 Hz	Odd feeling that she will pass out	52 / SD / VPA 54 / R / no AED	No No	< 5 years
11/F/27	24 / R	Small OS only in sleep and HV	Occipital to central / 18-30 Hz	"Overwhel- ming sensation"	25 / SD / no AED	posterior to frontal ("over- powering")	> 3 years
12/F/42	36 / R	-	Occipital spike-wave / 10-25 Hz	Cephalic sensation & strain in eyes	38 / SD / VPA-LEV	No	< 2 years
13/M/44	35 / R	-	Occipital to posterior temporal spike- wave / 15-18 Hz	Cephalic feeling at the back of head	43 / SD / no AED	Declining	> 8 years

Table 2. (Continued).

Patient/ Sex/ Age	Age at first EEG / Type	Interictal EEG abnormalities	First EEG (PPR / range)	Reported PPR-asso- ciated symptoms	Age at last EEG / type / AED	PPR response	Estimated* persistence of PPR
14/M/40	38 / R	-	Occipital to central / 20-30 Hz	"Jumping" images and loss of focus	-		Unknown
15/M/35	32 / SD	OS on eye closure after awakening and in HV	Occipital to central / 14-25 Hz	-	35 / R / no AED	No	< 3 years

*From the very first photogenic seizure; **This patient had routine EEGs at age 42 and 43 on VPA at 300 mg bd that had shown PPR; R: routine EEG; SD: EEG after partial sleep deprivation; OS: occipital spikes; IPS: intermittent photic stimulation; HV: hyperventilation; AED: antiepileptic drugs; VPA: valproate; LEV: levetiracetam.

The mother of Patient 7 reported similar visual symptoms as her daughter when she was in her late 20s, but without loss of consciousness. A first aunt of Patient 10 had "epilepsy", while a paternal aunt of Patient 14 had seizures at age 40, controlled with valproic acid (VPA). Patients 9 and 10 reported head injuries two weeks and a few months before seizure onset, but there were no antecedents for epilepsy in any of the 13 other patients. None had history of alcohol abuse or took any illicit drugs.

Age at seizure onset

Ten patients had their first symptoms within a month before their initial assessment at the first-seizure clinic, while five (Patients 2, 4, 6, 10 and 14) reported previous similar seizures 1-15 years before our first assessment which, however, occurred when the patients were >20 years of age (ages: 22-47; *table 1*). Therefore, the onset of photically-induced seizures ranged from 22 to 47 years (mean: 34; median: 33; SD: 8), age at first evaluation from 24 to 48 (mean: 36; median: 36; SD: 8), and follow-up from 1 to 14 years (mean: 4; median: 3; SD: 4).

Seizure provocation and triggers

All 15 patients reported exposure to environmental sources of light at the time of their seizures, while five had additional spontaneous seizures (*table 1*). Triggers included strobe lights in night clubs or flickering fluorescent lights in shops (Patients 1-3, 7-9, 12, 14 and 15), sunlight through fences and trees (Patients 9 and 13), sudden exposure to bright sunlight from darkness (Patient 4; *supplementary data*), or working long hours with a PC (Patient 6; a graphic designer, and Patient 11; a biology researcher who developed symptoms at age 24, a few months after she started her post-doctoral position). Patient 10 had visual symptoms only when watching TV and Patient 5 had his only seizure on a

sunny morning while crossing a bridge over a river. Conditions that could have lowered seizure threshold at the time of the seizure(s) were identified in 10 patients and included sleep deprivation, tiredness and stress.

Seizure types and semiology

All patients had focal seizures and 13 had secondary generalized convulsions; Patients 4 and 9 had only focal seizures. Initial symptoms were indicative of posterior onset in most patients, including complex (formed) visual hallucinations, visual illusions and oculomotor symptoms; Patients 9, 11 and 13 reported non-specific ictal symptoms, including cephalic sensation (Patients 9 and 13) and headache (Patient 13), while Patient 12 described initial (conscious) head and upper body version but no other symptoms. Elementary visual hallucinations or strictly deficient visual symptoms, such as scotomata, hemianopsias or transient amaurosis, were not reported by any patient (*table 1*).

EEG

Interictal EEG

With the exception of mild non-specific temporal theta activity in some of the older patients, background was in all patients normal. Small occipital spikes occurred in four patients, all during sleep-deprived EEGs. No generalized spike-wave discharges (GSWD) occurred (*table 2*).

IPS

Posterior PPR, mainly on eye closure and with eyes closed, occurred in all patients with variable propagation to temporal and central areas; frontal areas were involved in Patients 4 and 11 (*table 2; figures 1 and 2*). PPR outlasted IPS only in Patients 1 and 15. The range

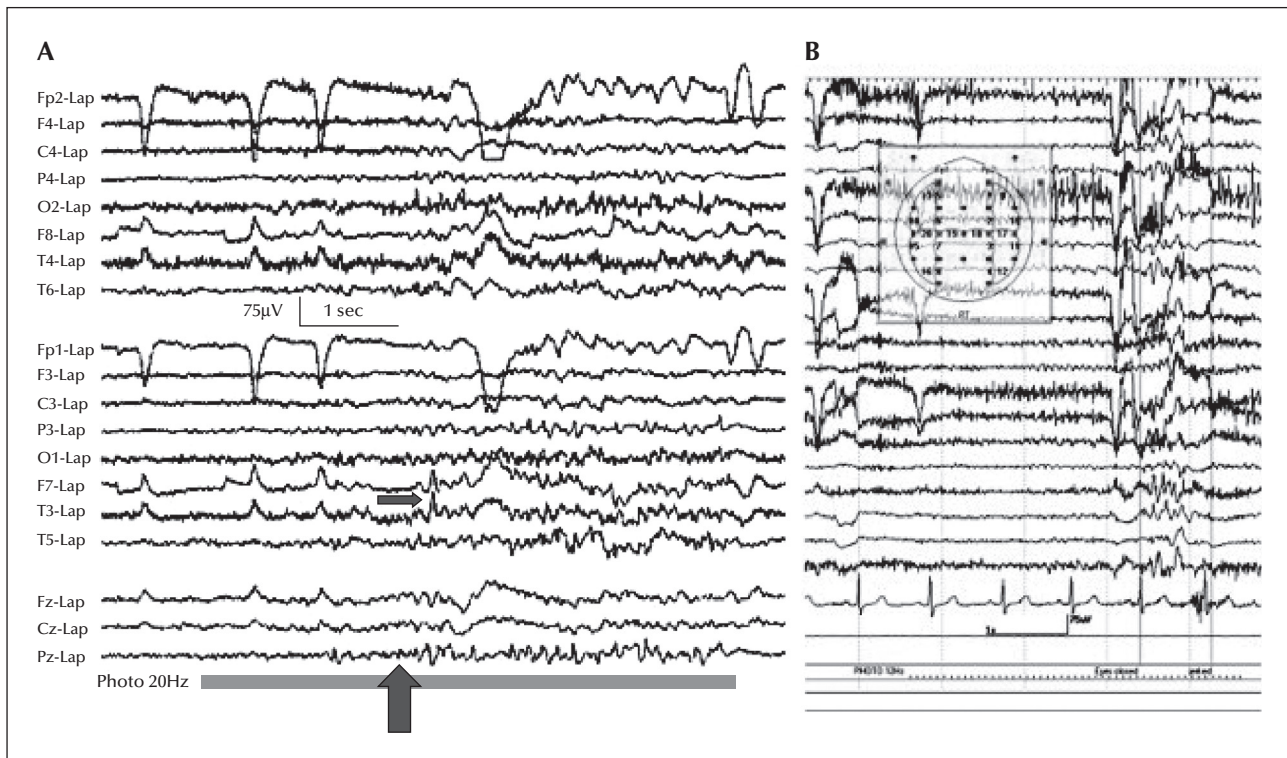


Figure 1. (A) Standard video-EEG of Patient 3 at the age of 47 years, with no AED. Posterior PPR, while eyes were open, were more evident over Pz (vertical arrow) and the right occipital area, although they could be traceable slightly earlier. Shortly after, epileptic activity spreads over the left temporal areas, apparently accounting for the dysphasic symptoms of this patient (Patient 3; *supplementary data*). (B) SDEEG in Patient 4 at the age of 48 years, with no AED. Posterior PPR on eye closure, spread to bilateral temporal, parietal and central areas, more on the right; the patient reported a body jerk that was evident on the video and the ECG lead (Patient 4; *supplementary data*).

of EEG photosensitivity was from 8 to 30 Hz; the maximum individual range was 18 Hz and the minimum 2 Hz. Symptoms associated with the PPR were triggered in 11 patients and were similar to their habitual symptoms in six. Follow-up EEGs, performed in nine of 15 patients, showed that PPR disappeared in five (of whom three had received AED treatment), but was persisting in four, of whom only one was treated (*table 2*).

Imaging

Brain MRI was normal in 14 patients; Patient 9 had normal head CT.

Number of seizures and response to treatment

Three patients had a single seizure, nine had 2-5 seizures, and three had multiple seizures. Seizure frequency before diagnosis ranged from >10 within two years (Patient 11) to one every five years (Patients 3 and 4) with only five patients having more than one/year. All patients received appropriate advice about seizure prevention, including watching television from an appropriate distance with good ambient light, taking regular breaks when working with computers,

avoiding conditions known to lower the epileptogenic threshold (such as sleep deprivation, tiredness and stress), covering one eye with their palm when exposed to unexpected lights, and even using appropriate lenses (Verrotti *et al.*, 2012). Seven patients received treatment (VPA at 200 mg bd to 500 mg bd in five, VPA and levetiracetam [LEV] in one, and lamotrigine [LTG] at 50 mg bd in one). None of the treated patients had further seizures within two to six years of follow-up (mean: 4.5; median: 5 years); in two of them (Patients 4 and 10), it was possible to stop VPA treatment. Only one of the eight untreated patients continued with occasional visual seizures, particularly when sleep-deprived or tired (Patient 11; *table 1*).

Group 2: Patients with adult-onset idiopathic (genetic) generalized epilepsies (IGE/GGE), associated with photoparoxysmal response (PPR)

This group consisted of eight patients with generalized tonic-clonic seizures (GTCS) alone (seven females and one male) and a man with juvenile myoclonic epilepsy (JME). The age at seizure onset ranged from 20 to 28

(mean: 24; median: 24; SD: 2), the age at first clinical assessment and EEG evaluation ranged from 20 to 32 (mean: 26; median: 25), and the follow-up from 1 to 7 years (mean: 5; median: 4). Brain MRI was normal in all. Three patients had a first-degree relative with seizures (two with GTCS and one with febrile convulsions). The number of GTCS ranged from 1 to 8 (mean: 3; median: 1) and only one patient reported that one of her two GTCS was possibly triggered by environmental light. Another patient reported that in the second of her two seizures her vision “switched rapidly between on and off, as though bright light was covering my visual field” for a few seconds before losing consciousness; an overall pleasant sensation that she was unable to stop. She could not recall a light trigger. The first SDEEG showed brief/abortive GSWD in five patients, posterior or GSWD on eye closure in four, and occipital spikes during sleep and hyperventilation in one patient, while SDEEG was normal in two patients; eight patients had generalized PPR at between 12 and 30 Hz (including a brief absence associated with 3-Hz GSWD in the patient with the photically-induced seizure) and occipital PPR at between 20 and 30 Hz in one patient. One patient reported that she “felt mesmerized” during the PPR and had a jerk, whilst another felt “tensed up” without visible jerking on video. Of the six patients treated (three with LEV and three with VPA), five were seizure-free for 2-5 years (LEV was stopped in one), while one had annual GTCS associated with poor sleep hygiene and alcohol excess. One patient declined treatment and remained seizure-free for five years, and two were lost to follow-up after one and two years, respectively (both declined treatment). Follow-up EEGs, performed in eight patients after 2-7 years, showed that PPR disappeared in four of the treated patients and persisted in the other four (of whom two were treated).

The main differences between Groups 1 and 2 are shown in *table 3*.

Group 3: Patients with epilepsies since childhood and adolescence and late-onset photoparoxysmal response

This group included four patients who were followed clinically with EEGs for many years before they developed subclinical PPR, all after the age of 20 (see *supplementary data*).

Discussion

The demonstration of photoparoxysmal response on the EEG of adult patients referred due to a possible first epileptic seizure does not necessarily indicate adult-onset epilepsy; of our 30 patients, four had acute

symptomatic seizures and two had vasovagal syncope. While our four patients of Group 3 emphasize that PPR can occur late in the natural history of IGE/GGE and focal epilepsies (and possibly independently of the primary syndrome given the long lapse of time), our patient Groups 1 and 2 demonstrate that photosensitivity can be the primary cause of adult-onset epilepsy (Group 1) and also accompany IGE/GGE of adult onset (Group 2).

We identified a clinically and EEG homogenous group of 15 patients with first presentation of photically-provoked seizures in their adult life. None had any seizure symptoms before the age of 20, either spontaneous or in association with environmental sources of light, or acute symptomatic seizures, including those associated with alcohol withdrawal or intoxication (Beghi *et al.*, 2010). In each patient, all or almost all seizures were associated with environmental sources of light. Ictal symptoms were suggestive of primary activation of the occipital cortex with propagation to temporal or frontal areas; in most patients, seizures became secondary generalized. EEG showed sparse occipital spikes during sleep or after awakening in a quarter of patients, but GSWD were conspicuously absent even on SDEEGs. IPS consistently provoked posterior stimulus-independent PPR with variable degree of anterior spread in all patients, and was associated with symptoms in almost three quarters of them (*table 3*), replicating habitual ictal symptoms in a third (*tables 1 and 2*). A third of patients had positive family history of epilepsy and brain imaging was normal in all. In general, photically-induced seizures were infrequent and responded well to appropriate advice and to moderate doses of VPA. This focal clinical/EEG photosensitivity phenotype contrasts with another type of adult-onset photosensitivity, which is associated with GGE/IGE (our Group 2) (*table 3*). Here, excitation of the photosensitive occipital areas does not remain regional as in the first group, but it rapidly engages in the already existing hyperexcitable thalamocortical circuit triggering generalized PPR and, infrequently, seizures. Despite being generalized, photosensitivity contributed little to the overall clinical presentation of these patients, and therefore may have limited impact on the outcome that appears to primarily depend on the clinical syndrome. On the other hand, the two groups shared a number of features: common seizure threshold modulators (such as sleep deprivation), positive family history, normal neurological state and brain MRI, a generally benign course, and favourable response to similar AEDs, mainly VPA (Harding *et al.*, 1978).

Our Group 1 is similar to the syndrome of idiopathic photosensitive occipital lobe epilepsy (IPOE) of childhood (Guerrini *et al.*, 1995; Yalçın *et al.*, 2000; Politi-Elishkevich *et al.*, 2014) in many important ways.

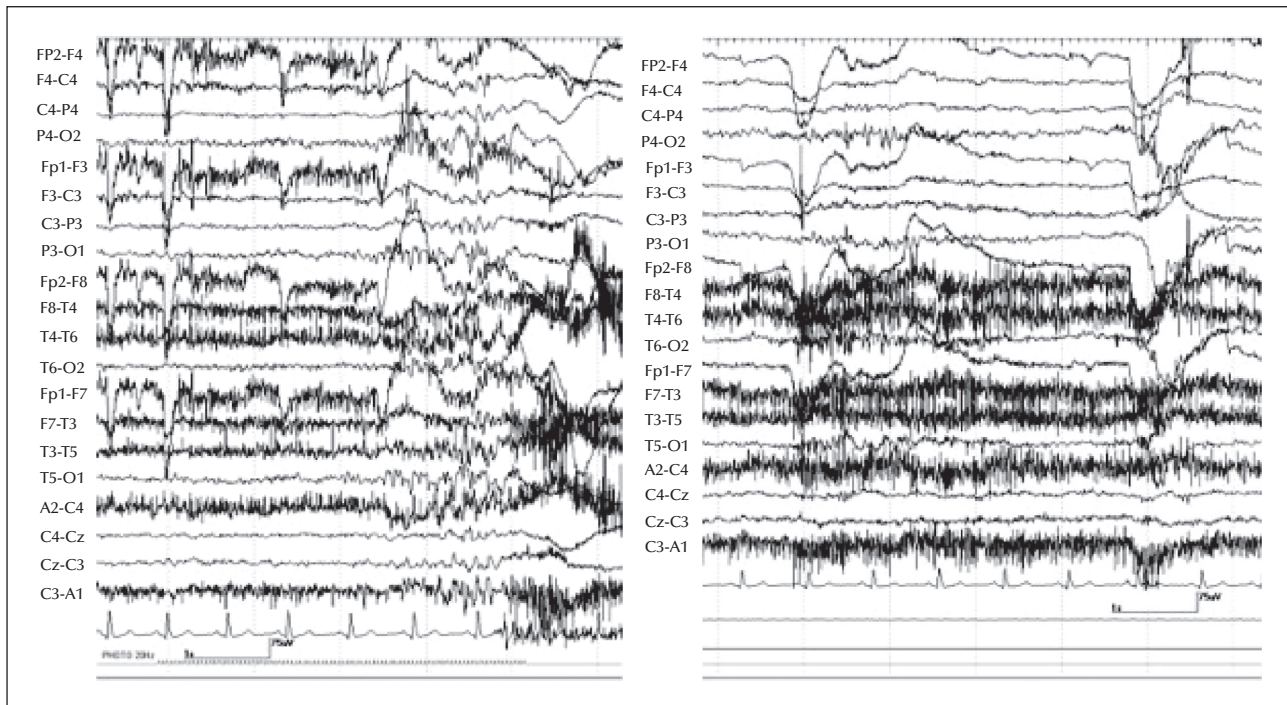


Figure 2. SDEEG in Patient 7 at the age of 33 years, with no AED. She had two seizures at age 31 and 33 when she was seen in our first-seizure clinic. Both started with her vision going “jumbled/swirly” then blurred, and her left arm twitched and she felt her head being pulled to the left, with disorientation and possibly unresponsiveness. During these two years, she also had a few visual episodes without impairment of awareness, all triggered by photic stimuli (strobe lighting in night clubs or sunlight through fences). Left trace: IPS at 20 Hz with posterior PPR spreading to temporal and central areas; the patient reported “jumbled/swirly” vision. She also had stimulus-independent occipital spikes at 12–18 Hz on eye closure, without associated symptoms. Right trace: eye closure with occipital spikes (R>L) after IPS. The EEG during sleep and hyperventilation was entirely normal.

Both conditions are characterized, exclusively or almost exclusively, by photically-induced seizures of occipital semiology and subsequent involvement of the temporal areas with secondary generalization in most patients, or, less frequently, with symptoms suggestive of temporal lobe involvement without preceding visual symptoms (Politi-Elishkevich *et al.*, 2014). Other common features include positive family history in 30–50% of patients and normal neurological state and brain MRI. There is agreement between all studies that IPOE is responsive to appropriate advice and antiepileptic treatment, and long-term outcome appears fair. Notwithstanding the clinical similarities, there are some EEG differences that may be age-related. For instance, PPR were typically posterior in the adult patients (only 2 of 15 had additional generalized PPR), but were more balanced in children; of the total 39 children described in the three series above, 26 had posterior and 27 generalized PPR. Also, spontaneous interictal epileptic discharges occurred more in children than in adults; occipital spikes were noted in 25 (and a few also had central-temporal spikes) and GSWD in 13 of the 39 children, while only four of our adult patients had rare occipital spikes (on SDEEG only), and none had

GSWD. Finally, the group range of photosensitivity appears wider in children (5–40 Hz in the series of Guerrini *et al.*, 1995) than in adults (8–30 Hz in this series).

Conclusions and remaining uncertainties

This work shows that photosensitivity can first occur in adult life and manifest, either exclusively or almost exclusively, with photically-induced focal seizures with secondary generalization or as an EEG, or less often, a clinical/EEG feature of GGE/IGE. With regard to everyday clinical practice, and particularly in the setting of the first-seizure clinic, the evidence from our patient Group 1 fills a diagnostic gap for those adult-onset focal epilepsies that are hard to diagnose and classify, either at the level of syndrome or that of aetiology. Given the initial focal seizure symptoms that may not always indicate an occipital onset, the lack of generalized PPR and the paucity of spontaneous interictal epileptic activity (unless SDEEG is performed), and normal brain MRI, most of these patients could be classified with late-onset posterior cortex or even

Table 3. Adult-onset epilepsies associated with photosensitivity.

	Group 1 (n=15)	Group 2 (IGE/GGE) (n=9)	
Age at seizure onset			
Mean	34	24	$p < 0.01$ ($z = 2.9516$)*
Median	33	24	
SD	8	2	
Range	22-47	20-28	
Gender (M/F)	9/6	2/7	NS
Photogenic seizures	15	1	$p < 0.0001^{**}$
GPPR	2	8	$p = 0.005^{**}$
Posterior PPR	15	1	$p < 0.0001^{**}$
Symptoms during PPR	11	1	$p = 0.0918^{**}$
Abnormal interictal EEG	4#	7†	$p = 0.0327^{**}$

*Mann-Whitney, 2-tailed; **2-tailed Fisher's exact test; #occipital spikes; †generalized spike-wave discharges

temporal lobe epilepsies of *unknown* (cryptogenic or probably symptomatic) aetiology and unpredictable prognosis. Yet, we present clinical and EEG evidence of a photosensitive occipital epilepsy syndrome of adult onset with good prognosis, with most patients requiring only mild and finite AED treatment or no treatment at all, as long as there are no additional spontaneous seizures. As there is evidence of genetic predisposition (apart from the photosensitivity itself, four of the 15 patients had a close relative with a history of epilepsy), the condition could be characterized as “possibly genetic (idiopathic) photosensitive occipital epilepsy of adult onset”, and be placed next to its paediatric/adolescence counterpart (Guerrini *et al.*, 1995) and together with the myoclonic epilepsy of adult onset (Gilliam *et al.*, 2000), the senior counterpart of juvenile myoclonic epilepsy.

A remaining question is whether adult-onset pure reflex photosensitive epilepsy always manifests with focal (occipital lobe) seizures. Adults with reflex photosensitive generalized epilepsy manifesting with generalized seizures (absences, myoclonic and GTCS) do exist, but in our experience their seizures start in childhood or adolescence and persist into adulthood. Some of these patients may experience additional focal photically-induced seizures, as may be the case for photosensitive patients with IGE (Hennessy and Binnie, 2000; Koutroumanidis and Smith, 2005; Gungor-Tuncer *et al.*, 2012), while some others with adult idiopathic (possibly genetic) reflex occipital epilepsy may report generalized seizures without initial “focal” symptoms when sleep-deprived or tired, although we have not yet encountered any patient with undisputable generalized photosensitive epilepsy of truly adult onset. However, present evidence is from a

single centre and more observations are needed to complete the spectrum of adult-onset photosensitive epilepsies

Supplementary data.

Summary didactic slides and supplementary data are available on the www.epilepticdisorders.com website.

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Learning points

A. Photosensitivity manifests clinically and electrographically (and peaks) during childhood and adolescence in the majority of genetically susceptible people, but it may do so later in adult life in a few patients who were not photosensitive before the age of 20 years.

B. EEG photosensitivity in the adult, referred due to a possible first seizure, does not necessarily indicate adult-onset epilepsy; acute symptomatic seizures and non-epileptic conditions should be carefully ruled out.

C. Photosensitivity can be part of idiopathic (genetic) generalized epilepsies of adult onset, but may also be the primary cause of newly diagnosed (reflex) epilepsy in adults in the form of idiopathic (genetic) photosensitive occipital epilepsy (IPOE).

D. Diagnostic criteria for the adult type of IPOE include:

1) Focal or secondary generalized seizures of occipital origin according to clinical symptomatology and EEG findings.

2) Typically posterior PPR in response to IPS.

3) Clinical evidence of occipital seizures associated with exposure to environmental visual stimuli; a point to remember is that overt clinical symptoms (such as unresponsiveness or secondary GTCS) could appear when patients are no longer exposed to photic stimulus, due to slow spread of seizure activity. Concurrently or alternatively to the historical clinical evidence, a clinical response to IPS with symptoms/signs suggestive of occipital lobe activation or temporal spread is also a criterion; this may or may not be the case for those seizures associated with environmental stimuli.

4) No symptoms before the age of 20, either spontaneous or in association with environmental visual stimuli/sources of light.

E. Diagnosis of IPOE in the adult with a first seizure is clinically important because of its fair prognosis. Standard advice about non-pharmacological preventive measures in daily life may be sufficient for full seizure control, however, when pharmacological treatment is required, response to moderate doses of antiepileptic medication of VPA or LEV is excellent.

TEST YOURSELF



(1) Do photically-induced focal seizures always manifest with visual symptoms?

(2) Does posterior EEG photosensitivity in adults always suggest previous clinical photosensitivity (associated with generalized photoparoxysmal response) for patients in remission?

(3) In photosensitive patients, it may sometimes be difficult to historically identify a cause-effect relationship between a possible visual trigger (exposure to lights) and a clinically overt seizure; can you suggest a possible reason?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".