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Evaluation of absences and myoclonic seizures in adults with genetic (idiopathic) generalized epilepsy: a comparison between self-evaluation and objective evaluation based on home video-EEG telemetry

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ABSTRACT

Objective. People with focal epilepsies are known to under-document their seizures, but there is no data on self-documentation in adults with genetic (idiopathic) generalized epilepsy (GGE/IGE). We assessed the accuracy of self-evaluation of typical absences (TA) or myoclonic seizures (MS) in adults with IGE based on home video-EEG telemetry (HVET).

Methods. Patients' own estimates were compared to the objective count of *definite* TA and MS, performed visually. We considered definite TA as generalized spike-wave discharges (GSWD) that met any of the following criteria: 1) coinciding with clear behavioural arrest on video, 2) followed after a few seconds by positive indication that an absence occurred, or 3) in the absence of video, consistently coinciding with clear motor arrest, as evidenced by interruption of continuous muscle activity. For each patient, we also classified *probable* TA as GSWDs that were longer than those corresponding to the shortest *definite* TA on HVET or based on the most recent sleep-deprived EEG (SDEEG).

Results. From the first 300 consecutive adults who had HVET, 24 had IGE with TA and / or MS; 23 were women. Only one patient had newly diagnosed IGE. Erroneous self-assessment of TA and MS was noted in 16/24 patients (66.7%). Seizures were overestimated in nine (37.5%) and underestimated in seven (29.2%). Only one patient (4.2%) documented all her TA and MS without false-positive estimates. Overestimation (but not underestimation) of TA on HVET could be predicted when patients reported daily or multiple weekly TA and a recent SDEEG was either normal or contained only subclinical GSWD (p=0.0095).

Significance. Under- and over-self-documentation of TA and MS occurred in two thirds of adults with GGE/IGE, with substantial impact on their outpatient management and treatment. Diagnostic HVET is a useful tool for the detection of erroneous self-evaluation in these patients.

Key words: over-reporting, under-reporting, absence status, sleep EEG, impairment of awareness

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Accurate seizure documentation in people with epilepsy is essential for their optimal management and treatment (such as dose reduction or even withdrawal of their anti-seizure drugs [ASDs] in drug-responsive patients, or intensification of treatment and even consideration of epilepsy surgery in drug-resistant patients). It is also important for clinical trials, seeking approval of new ASDs, for most of which a responder rate of ≥50% seizure reduction is the primary outcome measure [1].

In daily clinical practice, our periodic perception of the frequency of our patients' seizures (and therefore of their clinical course) relies mainly on seizure diaries, compiled at home. However, studies comparing patients' self-evaluation with various methods of objective evaluation have indicated that this can be problematic. According to a recent review, patients document fewer than 50% of their seizures, on average, and this self-documentation varies significantly over time [2]. The majority of these studies concerned patients with focal seizures, with or without impairment of awareness (IoA), and focal to bilateral tonic-clonic seizures, and only a few were conducted on (or have also included) children or adolescents with absences [3-6].

In recent years, diagnostic home video-EEG telemetry (HVET) has been used as a cost-effective alternative to classic in-patient video telemetry [7]. Its main indications include the differentiation of epileptic seizures from other paroxysmal events (such as psychogenic seizures, parasomnias *etc.*), seizure and epilepsy classification in patients with a clinical diagnosis of epilepsy but inconclusive standard and sleep-deprived EEG (SDEEG), and full electro-clinical characterization of patients already diagnosed with a type of focal or generalized epilepsy. As HVET can be used to monitor seizures in patients' own environment without reduction of ASDs, this would seem appropriate also for seizure quantification. We prospectively sought to determine the accuracy of self-evaluation in all adults with genetic (idiopathic) generalized epilepsy (GGE/IGE) and persisting typical absences (TA) and / or myoclonic seizures (MS), who underwent HVET at St Thomas' Hospital.

Patients and methods

Of 300 patients who underwent HVET between 1st October 2018 and 31st December 2020, 24 were diagnosed with GGE/IGE manifesting with TA and/or MS. Twenty-three of them had IGE and one had generalized epilepsy, associated with Glut 1 deficiency. Syndrome diagnosis was made according to the recent ILAE classification [8] and is summarized in *table 1*, along with the pertinent clinical and previous SDEEG data and the primary reason for the HVET referral. Patients with generalized tonic-clonic seizures (GTCS) and those with phantom absences only [9] were excluded.

Home video-EEG telemetry (HVET) protocol

All our HVET studies are performed using XLTEK/Natus home video recording equipment. AMBU silver/silver chloride disposable electrodes are attached according to the 10-20 international system, using Elefix conductive paste, secured by 3-cm strips of Hypafix tape and held together by a double 5.5-size surgifix retaining bandage, tied comfortably under the chin. Bilateral mastoid, ECG and bilateral deltoid EMG electrodes are routinely used, while additional channels (tibialis anterior EMG, respiration belt, pulse oximetry and submental EMG) are used in patients with suspected sleep disorders.

We ask patients to attend the study with their close relatives or caregivers, who have witnessed their attacks. Clinical information, including previous medical correspondence and test results are usually available on the hospital electronic patient system, but full seizure history is taken anew, focusing on possible auras and other ictal symptoms and signs, as well as seizure timing and circadian distribution, circumstances, facilitators and possible triggers. We encourage patients to follow their usual daily routine as closely as possible for the duration of the study, typically between 48 and 72 hours, taking their regular ASDs. Patients are instructed to press the "event button" when they feel that a seizure is starting, while relatives and caregivers are encouraged to observe them throughout the study and for as long as possible to identify possible clinical events that may otherwise be missed by the patients. Patients and relatives are also instructed to document the time and describe the symptoms and the clinical manifestations of the seizures in a diary sheet, specifically designed for this purpose.

Following calibration and polygraphy signal testing and before the ambulatory part of the HVET, a 15-20-minute long baseline video-EEG recording is carried out at the EEG department, including hyperventilation (HV) and photic stimulation. In patients with known or suspected IGE, HV is performed at least twice with breath counting [10] to record and study absences, including their duration, the degree of IoA and possible ictal automatisms.

During the period of the HVET, we maintain communication with our patients over the phone to prevent and amend common and avoidable technical failures, such as the erroneous replacement of batteries in the headbox and the night-shot unit, and any detached sensors, *etc.*, and resolve possible tolerability issues.

▼ **Table 1.** Patient clinical characteristics.

Pt	Age /sex	Diagnosis	Onset/ follow-up (yrs)	Seizures	Last SDEEG	Current AED	Previous AEDs	Reported seizure frequency*	Reason for HVET	Seizure count on HTEV**	Seizure estimate
1	55/f	ASE	12/5	AS → GTCS	4 & 2yrs: brief sGSWDs	LEV, PB	TPM	AS monthly	Attempt to record AS; any unreported TA?	TA 0:0 [<20 brief sGSWD per 24h]	Appropriate
2	37/f	JME	13/3	MS, TA, GTCS	1y: brief sGSWDs; no TA	LTG, ZNS	LEV, VPA, CZP	MS weekly TA weekly GTCS 6/y	Confirm diagnosis of JME (with TA?)	TA 6:6 MS 2:2	Accurate
3	27/f	JAE	19/2	TA, GTCS	1y: abortive GSWDs	LTG	none	SF for 1 year	Confirm SF status to wean off LTG	TA 0:0 [few abortive GSWD]	Appropriate
4	44/f	JME	13/12	MS, GTCS (none over last 3 yrs)	8y: sGPSWD; no MS;	LTG, CZP	VPA, CBZ, LEV	MS weekly Possible new infrequent blank spells?	Frequency of MS New TA?	TA 0:0 MS 0:0 few sGSWD]	Appropriate
5	34/f	JME	8/10	TA, MS, GTCS (SF for 6yrs)	2y: normal	LEV	CLB	Possible TA? (2-3 over last 6months)	Recurrence of TA?	TA 0:0 [only epileptic K]	Appropriate
6	37/f	JAE	7/11	TA, GTCS	1y: TA (GSWD >5s)	LEV, CLB	LTG, LCS, VPA	TA weekly GTCS 3-4/year	Frequency of TA	TA 16:2 AS 1:0 [for 30min]	UR
7	24/f	JAE	11/8	TA, GTCS	4y: TA (GSWD >5s)	LTG	LEV	TA weekly 6 GTCS in total	Frequency of TA	TA 10:0 [also, several probable TA]	UR
8	18/f	Glut 1 deficiency (ADHD)	9m/17	TA, GTCS	3m: multiple sGSWDs	KD	VPA, LEV, TPM, ESM, LTG	TA weekly GTCS monthly	Frequency of TA	TA >20:3 [>100 probable TA (of ≥3s) in clusters]	UR
9	23/f	JAE	9/8	TA, GTCS	3y: no TA (one 3.5s sGSWD on awakening)	PER	CLB, LEV, ESX, VPA, TPM, LTG, ZNS	TA daily 3-4 GTCS/year	Frequency of TA	TA 10:4 (all by mother) [>50 probable TA > 5s, mainly in clusters on awakening]	UR
10	27/f	ELMA	4/6	TA, GTCS (none over last 6 yrs)	3y: EC-GSWD with ELM; patient was unaware	VPA (300bd)	LEV	TA daily	Burden of TA before reduction of VPA	TA >100:3 (all by husband)	UR

▼ **Table 1.** Patient clinical characteristics (*continued*).

Pt	Age /sex	Diagnosis	Onset/ follow-up (yrs)	Seizures	Last SDEEG	Current AED	Previous AEDs	Reported seizure frequency*	Reason for HVET	Seizure count on HTEV**	Seizure estimate
11	23/f	JME	14/9	TA, MS, GTCS,	1y: brief sGSWDs; no TA or MS	LTG, VPA (200od)	LEV, VPA (higher doses)	MS daily / weekly Long absences weekly 1-2 GTCS/year	Burden of MS and TA while tapering VPA	MS 6:0	UR
12	23/f	JAE	15/8	TA, GTCS	4y: on VPA 200bd only sGSWDs	LTG, VPA (100bd)	VPA (higher doses)	SF for 2 years	To confirm SF status while tapering VPA	TA 2:0 [> 50 probable TA >3s / 24h]	UR
13	22/f	JAE	11/10	TA, GTCS	11m: only sGSWD	VPA (800-300)	PGB	TA weekly, in clusters	Burden of TA before reduction of VPA	TA 0:2 [infrequent sGSWD]	OR
14	25/f	CAE	4/2	TA, GTCS (SF since age 16)	2m: normal	VPA (150bd)	VPA (higher doses)	TA daily since VPA was reduced from 300bd	Burden of TA while tapering VPA	TA 0:15 [no GSWD]	OR
15	22/f	JME	7/11	TA, MS, GTCS	2y: abortive GSWDs	VPA (700bd), LTG	none	TA daily MS daily GTCS annually	Burden of TA / MS before reduction of VPA	MS 0:3 TA 0:0 [few abortive GSWD]	OR
16	47/f	JAE	10/25	TA, GTCS (last >1yr ago)	2y: brief sGSWDs	VPA (500bd), LTG, ZNS	CBZ, LEV	TA daily	Burden of TA before reduction of VPA	TA 0:>10 (by mother) GTCS 0:1 (felt "groggy" in the morning) [only sGSWD]	OR
17	35/f	IGE-U	3/18	TA, GTCS (none for 12 yrs)	2y: frequent sGSWD; no TA	LTG, VPA (200od)	VPA (higher doses)	TA daily	Burden of TA while tapering VPA	TA 0:2 [abortive GSWD]	OR
18	42/f	JME	19/15	TA, MS, GTCS	8y: TA (GSWDs > 5s)	VPA (800bd), LTG	CLB, LEV	TA weekly A few GTCS/year	Burden of TA before reduction of VPA)	TA 0:0 [infrequent sGSWD]	Appropriate

▼ **Table 1.** Patient clinical characteristics *(continued)*.

Pt	Age /sex	Diagnosis	Onset/ follow-up (yrs)	Seizures	Last SDEEG	Current AED	Previous AEDs	Reported seizure frequency*	Reason for HVET	Seizure count on HTEV**	Seizure estimate
19	23/f	ELMA	7/9	TA (?SI), GTCS (none for >6yrs)	1y: ELM without GSWDs; normal EEG	LEV	VPA	TA daily	Confirm SF state	TA 0:16 reported by her mother [no EC related GSWD or other interictal GSWD]	OR
20	17/ m	Photo IGE	3/14	TA	2m: EC-sGSWD with ELM on awakening	ESX	None	TA daily	To quantify TA	TA 2:>50 reported by his mother [the 2 definite TA were associated with 5s GSWD]	OR
21	44/f	IGE-U	24/4	TA, GTCS	5m: single brief sGSWD	LTG	none	TA weekly	On-going TA?	TA 0:1 [infrequent sGSWD]	OR
22	33/f	CAE	3/25	TA GTCS (none for >10yrs)	5m: few sGSWD	LEV	VPA, LTG	TA daily	On-going TA?	TA 0:7 [abortive GSWD]	OR
23	23/f	JAE	22/1	TA, GTCS	7m: only sGSWD	LTG, CLB	none	Weekly long blank spells and 2 GTCS over 1 year	To confirm and quantify TA	TA 0:0 [no GSWD]	Appropriate
24	17/f	CAE	6/11	TA, GTCS (none for 7yrs)	1y: sGSWD; no TA	LEV, LTG	CLB, VPA	TA daily	To confirm & quantify TA	None TA 0: 0 [8 abortive GSWD]	Appropriate

*Based on patients/relatives for the few months before HVET.
**Ratios are based on *definite* TA (see methods); probable TA and other EEG findings are included in square brackets.
HVET: home video EEG telemetry; AS: absence status; ASE: absence status epilepsy; sGSWD: subclinical generalised spike wave discharges; TA: typical absences; MS: myoclonic seizures; GTCS: generalised tonic clinic seizures; SF: seizure-free; KD: ketogenic diet; NREM: non-rapid eye movements; OR: over-reporter; UR: under-reporter; ADHD: attention deficit hyperactivity disorder; EC: eye closure; ELM: eyelid myoclonia; LEV: levetiracetam; LTG: lamotrigine; ZNS: zonisamide; VPA: valproic acid; CLB: clobazam; CZP: clonazepam; ESM: ethosuximide; PER: perampanel; PB: phenobarbital; CBZ: carbamazepine; PGB: pregabalin.

We download and analyse the acquired data after the end of the HVET and, when needed, conciliate any discrepancies between patients' documentation on the event sheet and the video-EEG evidence over the phone.
We interpret the HVET studies, taking into account the findings of the baseline video-EEG and, for patients who have been followed in our department, the electroclinical manifestations of previously recorded seizures.

Objective identification of typical absences (TA) during HVET

In all types of ambulatory EEG recording, quantification of TA is inevitably hampered by the inability to directly assess awareness during generalized spike-wave discharges (GSWD) and therefore distinguish them from subclinical paroxysms (sGSWD). Whereas in the EEG department IoA can be identified using specific clinical protocols at different levels of complexity [10], in HVET, one has to rely on rather "crude" evidence. For instance, a *definite absence* is positively indicated when a GSWD coincides with sudden behavioural arrest, clearly visible on the video, or - in the absence of conclusive video evidence - by the relevant notification from a closely observing relative, made shortly after the suspected EEG discharge. However, this limited range of diagnostic criteria *alone* would lead to "objective" underestimation of the actual seizure frequency. GSWDs that *can* correspond to TAs often occur while patients are resting, watching TV or reading, or are outside the camera's view and, being so brief, they can be easily missed even by the most attentive and dedicated relative (*probable absences*). On the other hand, the duration of the GSWD, *per se,* does not accurately indicate whether the discharge is associated with IoA, or not. IoA can occur from the first second of the discharge [11] and therefore may characterize GSWD as short as two seconds [9, 12], or be undetectable even using the most sensitive clinical assessment (*i.e.* breath counting) for longer GSWD [9]. Identification of absences at home that would pragmatically best approximate their true frequency should take into account both "*definite*" and "*probable*" absences, which – for the purpose of this study – we defined as follows:

- ***Definite absences (when one of the following criteria is met):***

- Clear behavioural arrest on video that coincides with a GSWD (*figure 1, upper trace*).
- Positive indication by the attending relatives (or the patient) that an absence occurred, shortly (within a few seconds) after a GSWD, with or without video evidence, and irrespective of its duration (*figure 2*).
- In the absence of the above, clear motor arrest, evidenced by interruption of ongoing muscle activity on EMG polygraphy, strictly during the duration of a GSWD, and seen more than once (*figures 3, 4; lower traces*).

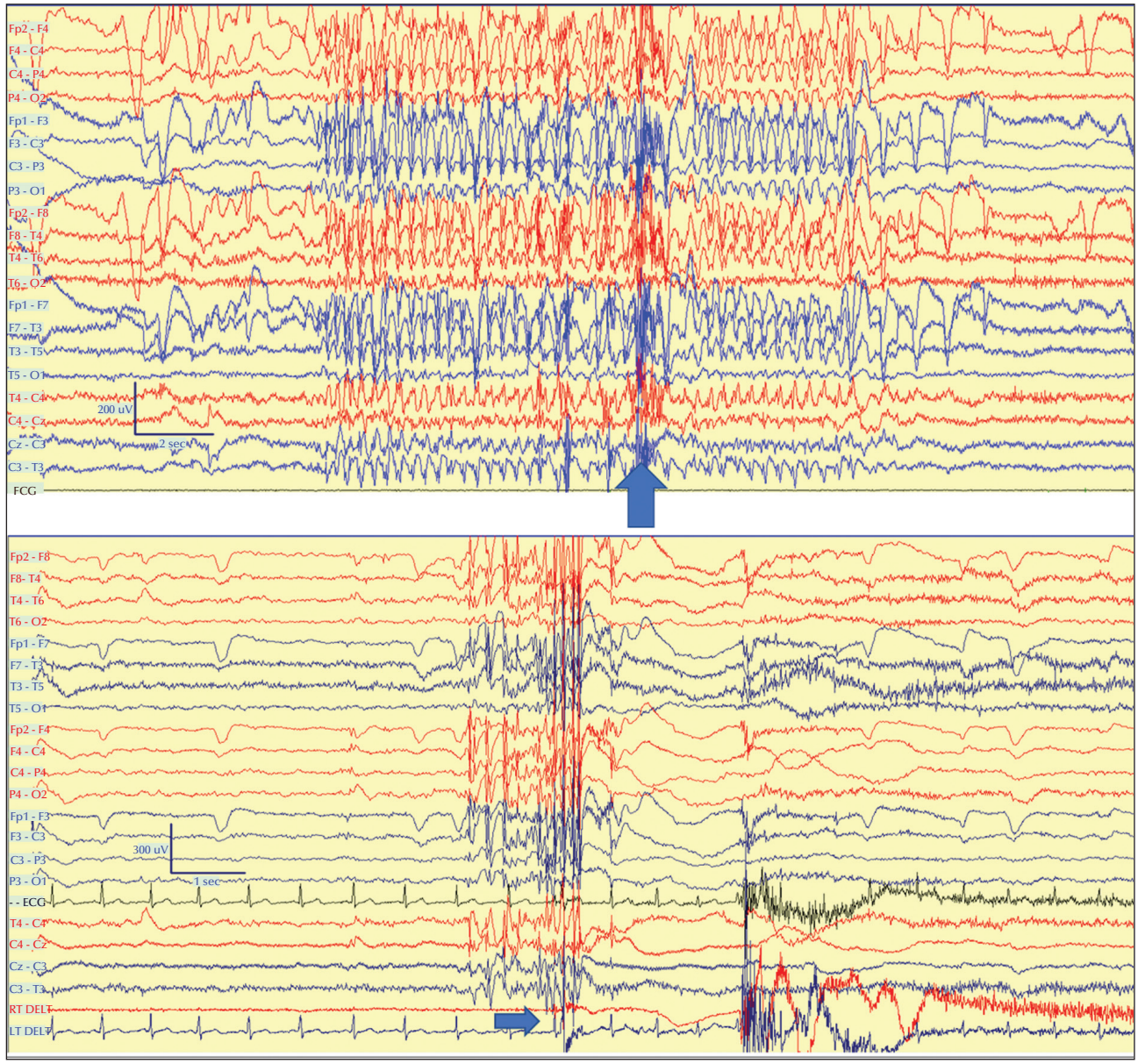
- ***Probable absences:***

- For each patient, we defined probable absences as GSWDs with duration longer than, or equal to, those associated with the shortest TA based on the *most recent* video SDEEG, or the shortest definite TA based on HVET (defined as above), rounded up to the next second. For example, for someone with TA known to associate with GSWD as short as 2.5 seconds, we considered all GSWDs lasting ≥three seconds as probable absences during the HVET (*figure 3, upper trace*).

To understand and classify possible errors in self-evaluation, we compared patients' estimates against their *definite* TA. For a closer approximation of the actual frequency of TA at home, we took both *definite* and *probable* TA into account. In this regard, we chose to err on the underestimation side and therefore excluded incompletely generalized discharges during wakefulness, irrespective of their duration; such discharges are associated with milder IoA [11] and may not be expected to be perceived by patients or relatives. We also excluded all GSWD during sleep and within periods of wakefulness after sleep onset, shorter than 30 seconds.

Objective identification of myoclonic seizures (MS) during HVET

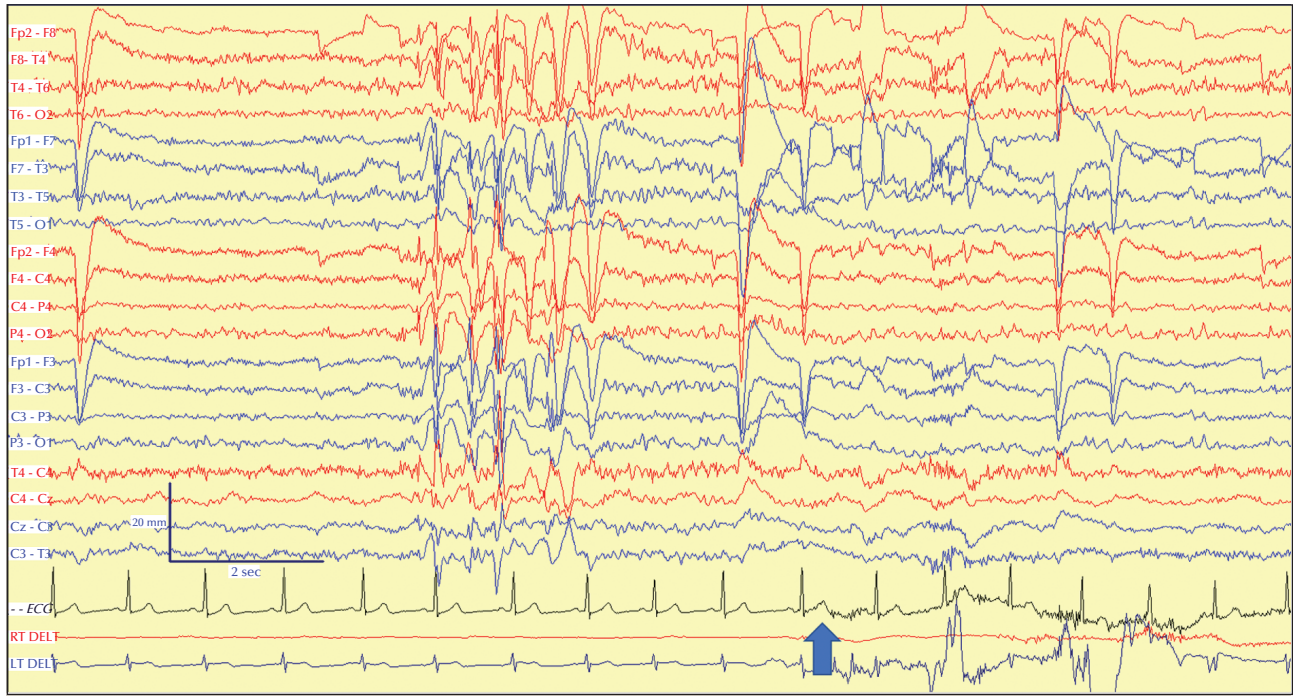
MS are identified when visible jerks are associated with GSWD or generalized polyspike-wave (GPSWD) with or without concurrent EMG potential from the contraction of the deltoids (*figure 1, lower trace*), or when (without clear video evidence) GSWD/GPSWD are associated with concurrent EMG bursts from the deltoids. Because mild MS may sometimes be perceived by some patients as an "inner feeling of jerk" without an overt jerk on video or EMG polygraphy, we were also prepared to consider brief GSWD/GPSWD without associated EMG potentials as MS, provided that the patient pressed the event button within a few seconds afterwards, identifying a typical myoclonic seizure. However, no such occasion arose in this cohort.
Statistical analysis: Categorical data were analysed using Fisher's exact test, with the level of significance set at $p<0.05$.



■ **Figure 1.** Upper trace: unreported absence in Patient 7. The vertical arrow marks the time of the ictal oral automatisms (for other clinical manifestations, see case vignette in text). Lower trace: typical MS in Patient 11 (see relevant case vignette in text). The seizure occurred as she was on the phone and the associated myoclonic jerk was clearly visible on video. The horizontal arrow shows the EMG potential from both deltoids. This patient missed all her MS.

Results

At the time of the HVET, the median age of the 24 patients (23 women) was 26 years (mean: 30.1; SD: 10.5; range: 17-55), the median epilepsy duration was 18 years (mean: 19.2; SD: 11; range: 1-43) and the median duration of their follow-up by us prior to the HVET was 9.5 years (mean: 10.17; SD: 6.46; range: 1-25); only one patient had newly diagnosed IGE (a year before her HVET). The mean duration of the HVET was 47.5 hours (median: 47; max: 72; min: 23) and the quality of the EEG and video recordings was good.



■ **Figure 2.** Brief 3-Hz GSWD during the 66-hour long HVET in Patient 2. Despite its brevity, the discharge is associated with her habitual unpleasant feeling of "light headedness", and is therefore identified by the patient. Note the ictal blinking and that three seconds later, she reaches for the sheet to document the event (arrow). She also pressed the event button a few seconds later (not shown here). Gain: 10µV/mm; LFF: 0.53Hz; HFF: 70Hz.

Clinical state prior to HVET

In their last outpatient clinical assessment before the HVET (*table 1*), 21 patients reported ongoing TA, of whom Patients 2, 4, 11 and 15 also reported daily or weekly MS. Of these 21 patients, 19 reported TA daily or several times per week, whereas Patients 4 and 5 reported infrequent blank spells that had been occurring for only a few months before the HVET; Patient 4 did not report previous TA, while Patient 5 had been seizure-free for six years. In addition to the patients above, Patient 1 had monthly episodes of absence status, sometimes ending with a GTCS, but had never complained of possible absences, and the remaining two (Patients 3 and 12) reported no seizures for one and two years, respectively. Twenty-three patients reported GTCS, either in remission or still ongoing.

At the time of the HVET, nine women (Patients 10-18) were on valproate acid (VPA), of whom five were on their regular doses (Patients 10, 13, 15, 16 and 18). The dose of VPA was being reduced in the other four women (*table 1*).

Pre-HVET seizure types and frequencies and the pertinent clinical data were confirmed at the EEG department on the day of the HVET set up.

Previous EEG findings

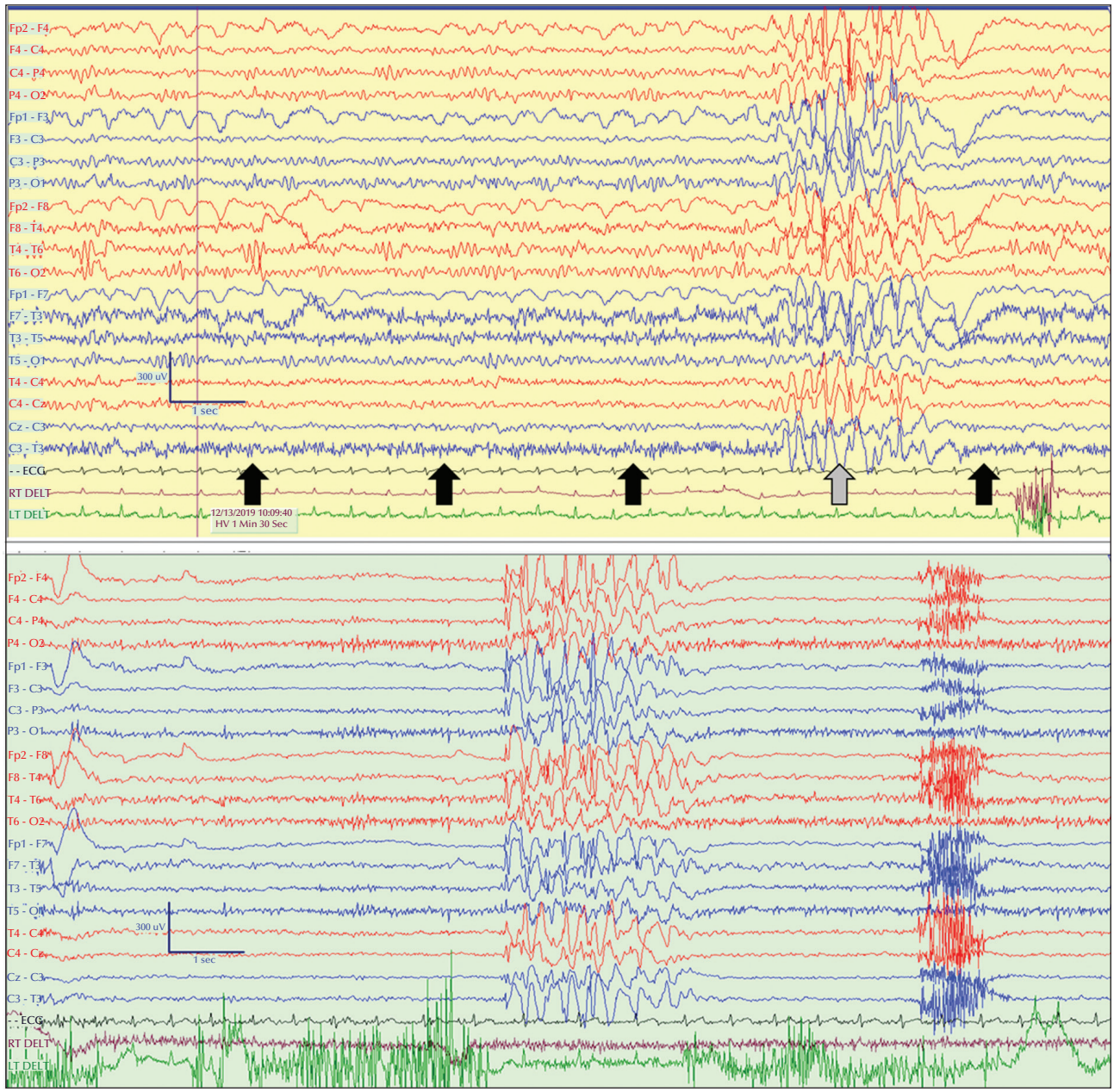
The timing of the most recent SDEEG and its findings are shown in *table 1*. The median time before the HVET was one year (mean: 2.06; SD: 2.09; min: 2 months; max: 8 years). The SDEEGs recorded TA in five patients, abortive or brief subclinical GSWD (sGSWD) in 16 and were normal in three patients.

Psychiatric comorbidity

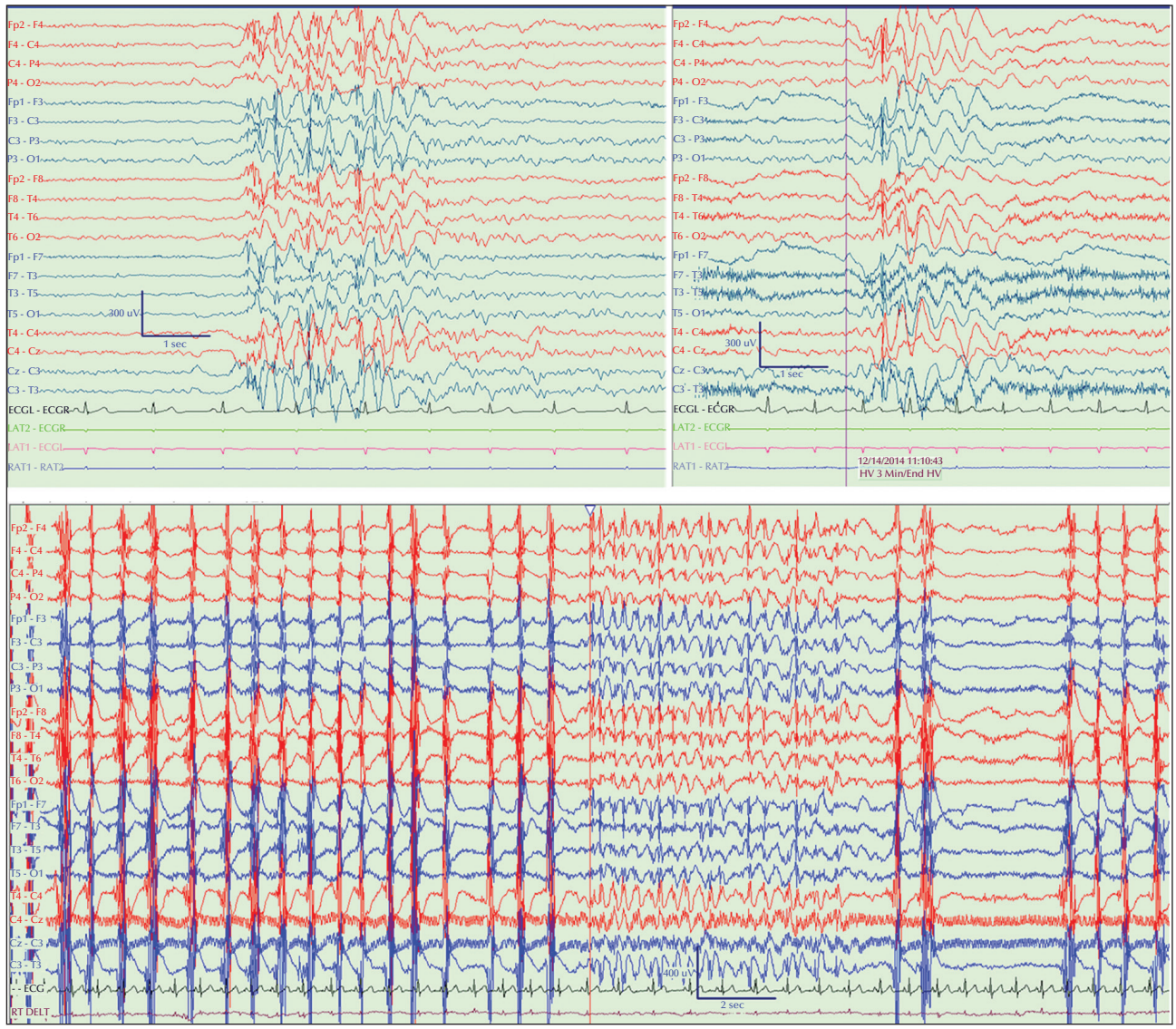
Patients 2 and 15 had depression and Patients 13 and 21 had anxiety disorder (post-traumatic in the latter). Self-induction was suspected in Patient 19.

Self-assessment during HVET by patients and their relatives

The HVET objective seizure count against patients' self-assessment and the clinical impression for each patient are presented in the last two columns of *table 1*. Overall, only one patient accurately reported all her TA and MS without false positive estimates (4.2%; Patient 2) (*table 1, figure 2*), one had correctly indicated that she was seizure-free (Patient 3) and another had rightly



■ **Figure 3.** Upper trace: a 2.5-second TA in Patient 8 was recorded during hyperventilation with breath counting on baseline video-EEG, just before the ambulatory part of the HVET. The regular rate of her sequential breathing, shown by the first three black arrows, is apparently distorted by the GSWD. The grey arrow shows the time her next breath was expected and the black arrow on the right, the time it actually occurred. The patient felt this delay as she smiled shortly afterwards. Lower trace: a longer discharge during the HVET, associated with a similar motor arrest (note the pause of EMG activity from the deltoids). The patient was not in view of the camera on this occasion.



■ **Figure 4.** Upper trace: subclinical GSWD in sleep (left) and during hyperventilation with breath counting on awakening on baseline video-EEG, just before the HVET, in Patient 9. Previous video EEGs had recorded TAs >4-5 seconds. Lower trace: motor arrest over the duration of a long GSWD, lasting >6 seconds, during the ambulatory part. Similar motor arrests occurred with other GSWDs.

denied any history of TA (Patient 1). Nine patients over-reported their seizures (Patients 13-17 and 19-22) and seven were under-reporters (Patients 6-12), of whom Patient 12 believed that she was entirely seizure-free for the last two years. Of the remaining five patients, who did not have any TA during the HVET and did not report any, two had volunteered possible infrequent blank spells of late onset (Patients 4 and 5), but three (Patients 18, 23 and 24) had complained of weekly or even daily TA for the few months prior to the HVET. Although these three patients were probably over-reporters, the notion was not supported by the HVET findings and they were not classified as such. Psychiatric comorbidity was present in four over-reporters.

After the HVET, VPA was stopped in Patients 11, 12 and 14 (addition of clonazepam in Patient 11 and increase in dose of lamotrigine [LTG] in Patient 12) and was reduced to 300 mgbd in Patient 13. The remaining five patients declined any VPA dose reduction, fearing that their GTCS would either worsen or relapse.

▼ **Table 2.** Findings based on the most recent SDEEG *and* reported frequency of TA before the HVET in the three self-evaluation groups (24 patients).

	TA on SDEEG *and* weekly / daily TA	TA on SDEEG *and* No (or infrequent) TA	No TA on SDEEG *and* weekly / daily TA	No TA on SDEEG *and* No (or infrequent) TA
Appropriate (*n*=8)	1	-	4	3
Over-reporters (*n*=9)	-	-	9	-
Under-reporters (*n*=7)	3	-	3	1
	4	-	16	4

TA: typical absences; SDEEG: sleep-deprived EEG; sGSWD: subclinical generalised spike-wave discharges.

Prediction of erroneous self-assessment based on the findings of the most recent sleep-deprived EEG and patients' self-evaluation prior to HVET

Of the four possible outcomes based on these two variables, frequent (weekly or daily) absences based on self-evaluation and subclinical or abortive GSWD only based on the most recent SDEEG were the most prevalent and found in all nine over-reporters (*table 2*). This was also the only combination to predict overestimation (p=0.0095), but not underestimation (p=0.167) or misestimation (over- and under- combined; p=0.36). The results of the recent SDEEG alone (recorded TA vs. only sGSWD or normal) could not predict the occurrence of TA during the HVET (p=0.13), even when the two patients, with their most recent SDEEG eight years before the HVET (Patients 4 and 18) (*table 1*), were excluded (p=0.055).

Case vignettes

Patient 2 had a history of brief jerks since her primary school years and of GTCS since age 13. She also complained of brief blank spells that started in her mid-teens and were associated with a fleeting feeling of "light-headedness". Previous SDEEGs, including the baseline HVET recording, had shown brief subclinical or abortive GSWD, but no TA or MS. During the HVET, she had six of her typical "blank spells", associated with three-second GSWD (*figure 2*), and two MS that involved both her arms simultaneously and were associated with high-voltage GPSWD; she also had a number of sGSWD/GPSWD. She accurately identified all eight seizures. The HVET confirmed the diagnosis of JME with brief absences.

Patient 7 started having blank spells at the age of 11 years and GTCS at age 15. She had never been on VPA (because of obesity), while levetiracetam (LEV) induced severe depression. On high doses of LTG, she was reporting few and sporadic absences almost daily. She has had six GTCS in total, all upon awakening. Previous video-EEGs recorded long, but rather subtle TAs with momentary staring and some mouth automatisms. She also had TA during the HVET baseline recording, associated with 5.7-second GSWDs or longer. During the 48-hour HVET, she had 10 TA associated with >six-second GSWD. In one, she was holding a baby while maintaining a conversation with her mother. She momentarily stopped talking but carried on patting and kissing the baby during the seven-second long GSWD. In another TA, while singing, her voice fleetingly faded with some mouth automatisms during a 12-second long GSWD (*figure 1, upper trace*). She also had multiple *probable* TA (GSWD >six seconds). Neither she nor her family reported any seizure during the HVET.

Patient 8 was included in this series because her generalized epilepsy was indistinguishable from IGE, but was due to Glut 1 deficiency. She had been relatively well controlled on the ketogenic diet until two years before the HVET. She then started having weekly vacant spells and GTCS every two to three months, associated with gradual reduction of blood ketones from 4.5-6 mmol/L to 1 mmol/L. Previous EEGs had shown only subclinical GSWD. She had a 2.6-second absence during the HVET baseline video-EEG during hyperventilation with breath counting (*figure 3, upper trace*). During the 48 hours of the HVET, she had hundreds of TAs associated with GSWD of 3-5 seconds, including dense clusters within the first 90 minutes after morning awakening, at the rate of 1.3 GSWD/minute. She took no notice of any of these despite a number of brief but clear concurrent motor arrests (*figure 3, lower trace*). She only pressed the event button three times (also registering them on the event

sheet as "absences"), in each case in close proximity to abortive GSWDs.

Patient 11 started having myoclonic jerks at age 15, typically upon awakening. Her first GTCS occurred a year later and was preceded by a cluster of jerks. She also reported blank spells since her late teens. Initial treatment with LEV caused mood swings. When she was transferred to our adult epilepsy clinic, she was on LTG 100bd with good seizure control, and a sleep-deprived EEG had shown subclinical GSWD but no MS or TA. She was then lost to follow-up and when we saw her again at age 21, she was on VPA 200bd and LTG 125mg bd, reporting infrequent jerks and GTCS. A sleep-deprived EEG, a year before the HVET, showed no MS or TA. After reduction of the dose of VPA, she reported weekly jerks and long absences. The HVET was performed to gauge the frequency of her MS and assess for possible absences before completion of the VPA withdrawal. Over the 47 hours of the test, she had six MS that she did not report (*table 1, figure 1 lower trace*), but no TA. The dose of LTG was then increased and clonazepam was added before VPA was stopped, just as she became pregnant. She then had a few GTCS during her pregnancy on this regime.

Discussion

The main finding of this study, the first to quantify TA and MS in adults with GGE/IGE, is that erroneous self-evaluation of TA and MS was documented in 16 of the 24 patients (66.7%), as either overestimation or underestimation; 37% of patients were over-reporters and 29.2% under-reporters. One of the under-reporters believed she was seizure-free for over two years before the HVET. Only one patient (4.2%) was able to document all her TA and MS seizures without over-reporting. Compared to the HVET-estimated frequencies, the over-reported TA were up to 25-fold more frequent, while the under-reported TA were from < 10 to ≥100-fold less frequent.

We also found that overestimation of TA (but not underestimation) could be predicted when there was a discrepancy between several TA per week or daily TA based on self-evaluation and a recent SDEEG that was either normal or contained only subclinical/abortive GSWD (p=0.0095). However, a SDEEG without TA *alone* could not predict an uneventful HVET and therefore cannot substitute the latter when identification and quantification of TA are concerned. It is emphasized that the above evidence applies to SDEEG with HV on awakening and assessment of possible IoA during GSWD with breath counting or an equivalent [10].

Discrepancy in documentation of TA and MS

As a rule, *TA* are not associated with any warning or subjective ictal sensation and their duration is relatively short. Therefore, IGE patients may not report their absences due to a lack of perception, as is the case in patients with focal seizures and IoA from onset [13]. Sometimes, however, absences can be perceived indirectly as "missed time" or "impaired concentration" when patients are actively focused on a task, *i.e.* whilst talking or texting on their mobile phone. Also, a few patients may recognize their absences when they experience fleeting symptoms that have been previously recognized as ictal [14] (see also Patient 2, *figure 2*). Despite their increased attentiveness for the short period of the HVET, relatives may also miss absences during inevitable "off periods". An additional reason for the underestimation we noted in 30% of our patients is that TAs tend to become less frequent and, in some patients, more inconspicuous with advancing age [15, 16]. Despite the rather noticeable paucity of subsequent relevant clinical research, these early clinical observations [15, 16] would suggest that monitoring protocols that are appropriate for drug-naïve children and adolescents with absences [3] and in children with childhood absence epilepsy [6] are probably inadequate for seizure documentation and quantification in adults with persisting TA.

Overestimation of TA has been noted before [3], presumably because of over-attentiveness related to either parental concerns that treatment is sub-optimal or from a feeling of insecurity that possible absences may be missed. For example, momentary blinks or brief periods of natural absent-mindedness may trigger false-positive estimates.

For MS, one would expect a lower rate of misestimation by patients as, by definition, these seizures occur with clear consciousness and can be felt. Observations based on long follow-up periods in patients with JME have indicated that MS become less intense over the years [17] and patients are undoubtedly conscious of this change in their symptoms. *Overestimation* by adults with a long history of MS might therefore relate to misinterpretation of a non-ictal "inner feeling of jerking", possibly fearing that some of them will pass unnoticed; this might have been the case in our Patient 15. Other reasons for overestimation include hypnagogic jerks, periodic leg movements and tics.

For the same reasons, although *underestimation* of MS is not expected, it does occur, apparently in relation to non-attentiveness. The reasons for such, sometimes staggering, inattentiveness (as in our Patient 11, *figure 1 lower trace*) are unclear despite its early documentation in photosensitive patients during photic stimulation [18] and the relevant experience in clinical EEG departments. These patients appear to

not "register" the jerks, or they do but the intention to document them may become instantly forgotten. To explain unreported *focal* seizures, it has been hypothesized that those arising from the dominant side may impair verbal memory and therefore verbal recall and reporting [19], while those arising from the non-dominant side may cause transient anosognosia and secondary non-awareness of the transient neurological deficit [20]. It is possible that similar mechanisms may operate in patients with IGE, who fail to notice clinically obvious MS. The causal generalized polyspike-wave discharges may momentarily interrupt specific cortico-thalamic network circuits, impacting on analogous constituents of awareness to the same effect [21, 22], without causing the global loss of awareness that the 3-Hz GSWDs in TA are typically associated with.

Strengths and limitations

Our HVET methodology ensured that the recording conditions simulated real-life circumstances as close as possible. Arguably, however, the intensity of monitoring by the motivated relatives over 24-72 hours may have been higher than normal, which may in turn suggest that patients' self-evaluation, at the level of the routine periodic outpatient epilepsy clinic, may be even less accurate. Also, our primary findings are based on the quantification of *definite* absences, which we identified using robust criteria. Pragmatically, in order to have a better idea about the true frequency of absences at home, avoiding false positives hits by including GSWD that may be subclinical, we also calculated patients' *probable* absences. Because identification of absences based purely on GSWD duration is inaccurate [4, 9, 11], we did not use an arbitrary cut-off duration. Instead, we defined probable absences for each patient according to the GSWDs that were longer than those associated with IoA based on the most recent SDEEGs or the HVET itself (*i.e.* their definite TA).

There are two main limitations to this study. First, our findings apply to patients with chronic GGE/IGE. With the exception of Patient 23, the cohort did not contain newly diagnosed patients. Most had long follow-up by us and several sleep EEGs in our EEG department. However, at any rate, HVET is not considered as a first-line diagnostic EEG investigation, particularly for clinically suspected IGE. Second, HVET offers only a 48-hour "snapshot" view of patients' self-assessment. It is therefore uncertain whether these observations change with time, and if so, how.

We conclude that, similar to patients with focal epilepsies, erroneous self-evaluation of TA and MS occurs in the majority of adults with a long history of IGE, with significant impact on their treatment. Our findings indicate that diagnostic HVET is also a valuable tool to restore our evidence-based management when clinical and EEG follow-up cast doubts on patients' self-reporting. ■

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Disclosures.
None of the authors have any conflicts of interest to declare.

References

1. Ben-Menachem E, Sander JW, Privitera M, Gilliam F. Measuring outcomes of treatment with antiepileptic drugs in clinical trials. *Epilepsy Behav* 2010; 18(1-2): 24-30.

2. Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. *Lancet Neurol* 2018; 17(3): 279-88.

3. Browne TR, Dreifuss FE, Penry JK, Porter RJ, White BG. Clinical and EEG estimates of absence seizure frequency. *Arch Neurol* 1983; 40(8): 469-72.

4. Tatum WO 4th, Winters L, Gieron M, Passaro EA, Benbadis S, Ferreira J, Liporace J. Outpatient seizure identification: results of 502 patients using computer-assisted ambulatory EEG. *J Clin Neurophysiol* 2001; 18(1): 14-9.

5. Akman CI, Montenegro MA, Jacob S, Eck K, Chiriboga C, Gilliam F. Seizure frequency in children with epilepsy: factors influencing accuracy and parental awareness. *Seizure* 2009; 18(7): 524-9.

6. Glauser TA, Cnaan A, Shinnar S, Hirtz DG, Dlugos D, Masur D, *et al*. Ethosuximide, valproic acid and lamotrigine in childhood absence epilepsy. *N Engl J Med* 2010; 362(9): 790-9.

7. Brunnhuber F, Slater J, Goyal S, Amin D, Thorvardsson G, Freestone DR, *et al*. Past, present and future of home video-electroencephalographic telemetry: a review of the development of in-home video-electroencephalographic recordings. *Epilepsia* 2020; 61(Suppl 1): S3-10.

8. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, *et al*. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia* 2017; 58(4): 512-21.

9. Koutroumanidis M, Aggelakis K, Panayiotopoulos CP. Idiopathic epilepsy with generalized tonic-clonic seizures only versus idiopathic epilepsy with phantom absences and generalized tonic-clonic seizures: one or two syndromes? *Epilepsia* 2008; 49(12): 2050-62.

10. Koutroumanidis M, Arzimanoglou A, Caraballo R, Goyal S, Kaminska A, Laoprasert P, *et al*. The role of EEG in the diagnosis and classification of the epilepsy syndromes: a tool for clinical practice by the ILAE Neurophysiology Task Force (Part 1). *Epileptic Disord* 2017; 19(3): 233-98.

11. Browne TR, Penry JK, Proter RJ, Dreifuss FE. Responsiveness before, during and after spike-wave paroxysms. *Neurology* 1974; 24(7): 659-65.

12. Sadleir LG, Scheffer IE, Smith S, Carstensen B, Farrell K, Connolly MB. EEG features of absence seizures in idiopathic generalized epilepsy: impact of syndrome, age, and state. *Epilepsia* 2009; 50(6): 1572-8.

13. Blum DE, Eskola J, Bortz JJ, Fisher RS. Patient awareness of seizures. *Neurology* 1996; 47(1): 260-4.

14. Gungor-Tuncer O, Baykan B, Altindag E, Bebek N, Gurses C, Gokyigit A. Prevalence and characteristics of visual aura in idiopathic generalized epilepsy. *Epilepsy Behav* 2012; 25(4): 573-6.

15. Gibberd FB. The prognosis of petit mal. *Brain* 1966; 89(3): 531-8.

16. Gastaut H, Zifkin BG, Mariani E, Puig JS. The long-term course of primary generalized epilepsy with persisting absences. *Neurology* 1986; 36(8): 1021-8.

17. Baykan B, Altindag EA, Bebek N, Ozturk AY, Aslantas B, Gurses C, *et al*. Myoclonic seizures subside in the fourth decade in juvenile myoclonic epilepsy. *Neurology* 2008; 70(22 Pt 2): 2123-9.

18. Kasteleijn-Nolst Trenité DG. Photosensitivity in epilepsy. Electrophysiological and clinical correlates. *Acta Neurol Scand Suppl* 1989; 125: 3-149.

19. Inoue Y, Mihara T. Awareness and responsiveness during partial seizures. *Epilepsia* 1998; 39(Suppl 5): 7-10.

20. Detyniecki K, Blumenfeld H. Consciousness of seizures and consciousness during seizures: are they related? *Epilepsy Behav* 2014; 30: 6-9.

21. Guillery RW, Feig SL, Lozsádi DA. Paying attention to the thalamic reticular nucleus. *Trends Neurosci* 1998; 21(1): 28-32.

22. Kostopoulos GK. Involvement of the thalamocortical system in epileptic loss of consciousness. *Epilepsia* 2001; 42 (Suppl 3): 13-9.

TEST YOURSELF

(1) Why is it important to document seizures accurately?

(2) What are the factors that may suggest a patient is under or over-reporting absences?

(3) What are the reasons behind under and over-reporting of typical absences?

(4) What are the reasons behind under and over-reporting of myoclonic seizures?

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